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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Robert (Reg) Shiao Examiner #: 79521 Date: 11/17/06

Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/501,636 (2004)

Location (Bldg/Room#): REM (Mailbox #): 5A10 Results Format Preferred (circle): PAPER DISK

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5C18

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Cyclodextrin ketoacyde

Inventors (please provide full names): Catalano et al

Earliest Priority Date: _____ Pct/us03/01271 349812p1 2002

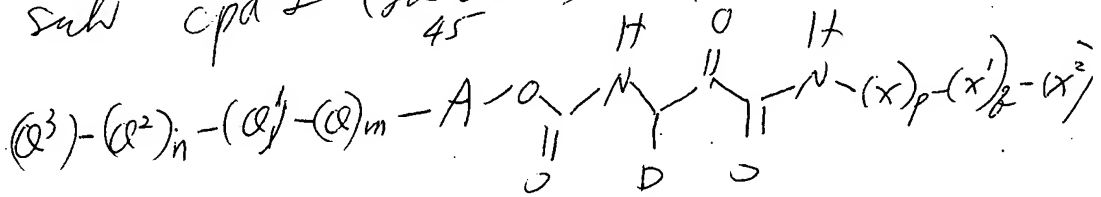
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

I. Sub cpd I (see claim 1)

45



* m is on 2, n is 1, p is 0 or 2, q is 0 or 1

Q_1 is C_3-C_7 cycloalkylene

Q_2 is OR, SR, N(R')R, R, R' are sub

Q_3 is aryl, heteroaryl

D is alkyl

X is C(R')(R'') R', R'' are sub

X' is C(O)OCH2

X^2 is aryl or heterocycle

II. method of use of cpd I

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STAFF USE ONLY

Searcher: Sabu Sheeva

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: 12/6/06

Date Completed: 12/6/06

Searcher Prep & Review Time: 60

Online Time: 32

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

_____ Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

__V__ STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial ____ Oligomer ____ Score/Length

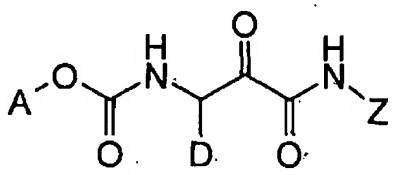
____ Interference ____ SPDI ____ Encode/Transl

_____ Other (specify)

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

1. (Currently amended) A compound of Formula (I):



(I)

or a salt, or solvate, ~~or physiologically functional derivative~~ thereof:

wherein

A is the group defined by (Q^3)-$(Q^2)_n$-(Q^1)-$(Q)_m$-, wherein

Q is CH_2 and m is 0, 1, or 2

Q^1 is C_3-C_7 cycloalkylene;

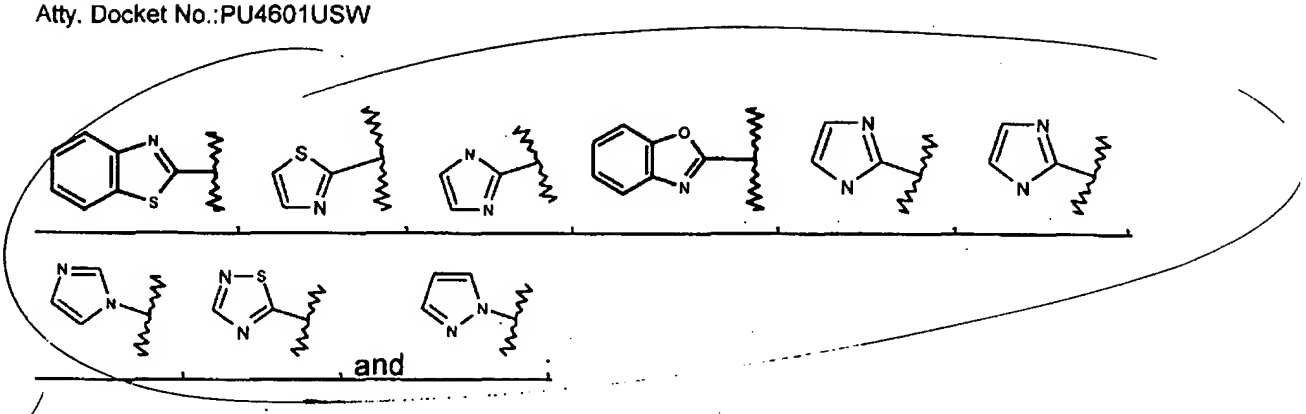
Q^2 is C_1-C_3 alkylene and n is 0 or 1, or

Q^2 is OR, where R is C_1-C_3 alkylene and n is 1,

Q^2 is SR, where R is C_1-C_3 alkylene and n is 1; or

Q^2 is N(R')R, where R' is hydrogen or C_1-C_6 alkyl, R is C_1-C_3 alkylene and n is 1; and

Q^3 is aryl, heteroaryl, or aryl or ~~hetero~~aryl substituted with at least one independently selected R^1 group, wherein said heteroaryl is selected from the group consisting of



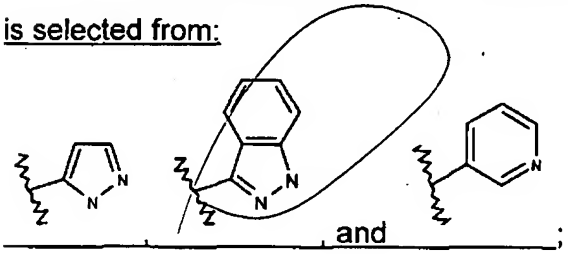
D is C_1-C_6 alkyl or C_1-C_6 alkyl substituted with $-NR^2R^3$;

Z is the group defined by $-(X)_p-(X^1)_q-(X^2)$, wherein

X is C(R')(R''), wherein R' is hydrogen or C_1-C_6 alkyl, R'' is hydrogen and C_1-C_6 alkyl, and p is 0, 1, or 2,

X^1 is $C(O)OCH_2$, wherein q is 0 or 1, and

X^2 is aryl, heteroaryl, or heterocyclyl wherein said hteroaryl or heterocyclyl is selected from:



R^1 is halo, C_1-C_6 alkyl, aryl, ~~heterocyclyl~~, or C_1-C_6 haloalkyl;

R^2 is hydrogen or C_1-C_6 alkyl;

R^3 is hydrogen, C_1-C_6 alkyl, $-C(O)R^4$, or $-S(O)_2NR^5R^6$;

R^4 is ~~heterocyclyl,~~ $-NR^5R^6$, and

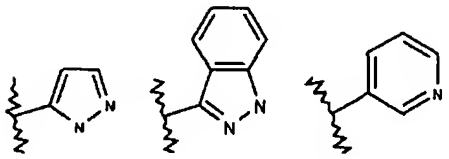
R^5 and R^6 are independently selected from hydrogen or C_1-C_6 alkyl.

2. (Cancelled)

3. (Cancelled)

4. (Cancelled)

44. (Original) A compound as claimed in claim 1, wherein X^2 is selected from the group



, or substituted derivatives thereof.

45. (Currently amended) A compound selected from the group consisting of:

1-benzylcyclobutyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate;

1-benzylcyclopentyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate;

benzyl(2S)-2-{[(3S)-3-({[(1-benzylcyclopentyl)oxy]carbonyl}amino)-2-oxoheptanoyl]amino}propanoate;

1-benzylcyclohexyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate;

(1-Benzylcyclobutyl)methyl(1S)-1-(oxo{[(1R)-1-phenylethyl]amino} acetyl) pentyl carbamate;

[1-(2-Phenylethyl)cyclobutyl]methyl (1S)-1-(oxo{[(1R)-1-phenylethyl] amino} acetyl) pentylcarbamate;

[1-(3-Phenylpropyl)cyclobutyl]methyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino} acetyl) pentylcarbamate;

(1-Benzylcyclopentyl)methyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl) pentyl carbamate;

~~(1-benzylcyclohexyl)methyl(1S)-5-[(4-morpholinylcarbonyl)amino]-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate;~~

~~[1-(4-Fluorobenzyl)cyclobutyl]methyl (1S)-5-[(4-morpholinylcarbonyl)amino]-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate;~~

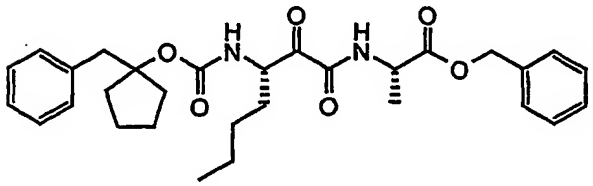
~~[1-(4-Pyridinylmethyl)cyclobutyl]methyl (1S)-5-[(4-morpholinylcarbonyl)amino]-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate;~~

~~[1-(3-pyridinylmethyl)cyclobutyl]methyl (1S)-5-[(4-morpholinylcarbonyl)amino]-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate~~;

nitrogen for 5 min, then 63.7 µL (493.9 µmol) of (S)-α-methylbenzylamine was added and the solution was stirred at –78°C for 15 min. The solution was concentrated and 5 mL of a 1 M solution of silver nitrate in tetrahydrofuran:water (4:1) was added and the mixture was stirred for 16 h at room temperature. The solution was extracted with ethyl acetate. The organic layer was washed with 10% citric acid, followed by saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with an ethyl acetate:hexanes solution (1:4) to give 33.4 mg (15%) of 1-benzylcyclopentyl (1*S*)-1-(oxo{[(1*R*)-1-phenylethyl]amino}acetyl)pentylcarbamate. R_f = 0.23 (1:4 ethyl acetate:hexanes); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.19 (d, J = 8 Hz, 1H), 8.31-7.11 (m, 11H), 4.98 (p, J = 8 Hz, 1H), 4.82-4.74 (m, 1H), 3.18 (s, 2H), 1.94-1.80 (m, 2H), 1.78-1.54 (m, 6H), 1.42 (d, J = 7 Hz, 3H), 1.40-1.16 (m, 6H), 0.81 (t, J = 7 Hz, 3H); HRMS $C_{28}H_{36}N_2O_4$+Na *m/z* 487.2573 $(M+Na)_{cal}$; 487.2568 $(M+Na)_{obs}$.

Example 3:

Benzyl (2S)-2-{[(3S)-3-({[(1-benzylcyclopentyl)oxy]carbonyl}amino)-2-oxoheptanoyl]amino}propanoate

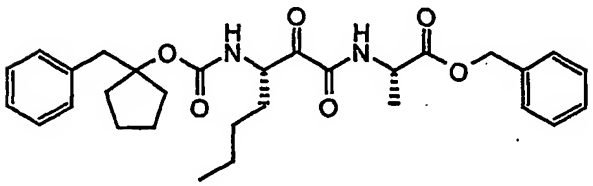


Ozone was bubbled through a solution of 205.1 mg (332.6 µmol) of 1-benzylcyclopentyl (1*S*)-1-[cyano(triphenylphosphoranylidene)acetyl]pentylcarbamate in 7 mL of dichloromethane at –78°C for 15 min. The solution was purged with nitrogen for 5 min, then 71.7 mg (332.6 µmol) of benzyl (2*S*)-2-aminopropanoate hydrochloride and 58.2 mL (332.6 mmol) of diisopropylethylamine were added and the solution was stirred at –78°C for 15 min. The solution was concentrated and 5 mL of a 1 M solution of silver nitrate in tetrahydrofuran:water (4:1) was added and the

nitrogen for 5 min, then 63.7 µL (493.9 µmol) of (S)-α-methylbenzylamine was added and the solution was stirred at -78°C for 15 min. The solution was concentrated and 5 mL of a 1 M solution of silver nitrate in tetrahydrofuran:water (4:1) was added and the mixture was stirred for 16 h at room temperature. The solution was extracted with ethyl acetate. The organic layer was washed with 10% citric acid, followed by saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with an ethyl acetate:hexanes solution (1:4) to give 33.4 mg (15%) of 1-benzylcyclopentyl (1*S*)-1-(oxo{[(1*R*)-1-phenylethyl]amino}acetyl)pentylcarbamate. R_f = 0.23 (1:4 ethyl acetate:hexanes); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.19 (d, J = 8 Hz, 1H), 8.31-7.11 (m, 11H), 4.98 (p, J = 8 Hz, 1H), 4.82-4.74 (m, 1H), 3.18 (s, 2H), 1.94-1.80 (m, 2H), 1.78-1.54 (m, 6H), 1.42 (d, J = 7 Hz, 3H), 1.40-1.16 (m, 6H), 0.81 (t, J = 7 Hz, 3H); HRMS $C_{28}H_{36}N_2O_4$+Na *m/z* 487.2573 $(M+Na)_{cal}$; 487.2568 $(M+Na)_{obs}$.

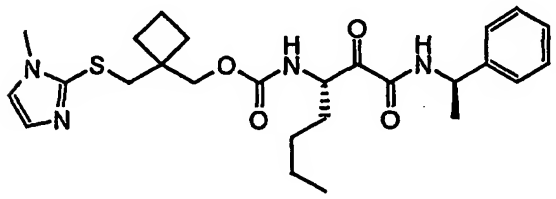
Example 3:

Benzyl (2S)-2-{[(3S)-3-({[(1-benzylcyclopentyl)oxy]carbonyl}amino)-2-oxoheptanoyl]amino}propanoate



Ozone was bubbled through a solution of 205.1 mg (332.6 µmol) of 1-benzylcyclopentyl (1*S*)-1-[cyano(triphenylphosphoranylidene)acetyl]pentylcarbamate in 7 mL of dichloromethane at -78°C for 15 min. The solution was purged with nitrogen for 5 min, then 71.7 mg (332.6 µmol) of benzyl (2*S*)-2-aminopropanoate hydrochloride and 58.2 mL (332.6 mmol) of diisopropylethylamine were added and the solution was stirred at -78°C for 15 min. The solution was concentrated and 5 mL of a 1 M solution of silver nitrate in tetrahydrofuran:water (4:1) was added and the

Example 19c: Preparation of (1-{[(1-methyl-1H-imidazol-2-yl)sulfanyl]methyl}cyclobutyl)methyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate



To a solution of 0.182 g (0.364 mmol) of (1-{[(1-methyl-1H-imidazol-2-yl)sulfanyl]methyl}cyclobutyl) methyl (1S)-1-(1-hydroxy-2-oxo-2-{[(1R)-1-phenylethyl]amino}ethyl)pentylcarbamate in 3 mL of dichloromethane cooled to –60°C was added 0.079 mL (0.91 mmol) of oxalyl chloride and 0.129 mL (1.82 mmol) of dimethylsulfoxide, followed by 0.204 mL (1.45 mmol) of triethylamine. After stirring for 15 min, the reaction was warmed to room temperature and applied directly to a silica gel column eluting with ethyl acetate to afford 0.052 g (29%) of (1-{[(1-methyl-1H-imidazol-2-yl)sulfanyl]methyl}cyclobutyl)methyl (1S)-1-(oxo{[(1R)-1-phenylethyl]amino}acetyl)pentylcarbamate as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.30 (m, 6H), 7.17 (d, J = 8 Hz, 1H), 6.98 (s, 1H), 5.41 (m, 1H), 5.23–5.11 (m, 2H), 4.16 (s, 2H), 3.58 (s, 3H), 3.36 (s, 2H), 2.07–1.89 (m, 6H), 1.48–1.16 (m, 6H), 1.56 (d, J = 7 Hz, 3H), 0.89 (t, J = 7 Hz, 3H). LC-MS m/z 501 (M+H).

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Bib Data Sheet

CONFIRMATION NO. 2460

SERIAL NUMBER	FILING OR 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/501,636	07/15/2004 RULE	514	1626	PU4601USW

APPLICANTS

John George Catalano, Durham, NC;
David Norman Deaton, Durham, NC;
Aaron Bayne Miller, Durham, NC;
Francis Xavier Tavares, Durham, NC;

**** CONTINUING DATA ***************************

This application is a 371 of PCT/US03/01271 01/15/2003 which claims benefit of 60/349,812 01/17/2002

**** FOREIGN APPLICATIONS *********************

Foreign Priority claimed	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ yes ☒ no 35 USC 119 (a-d) conditions met ☐ yes ☒ no ☐ Met after Allowance Verified and Acknowledged Examiner's Signature Initials	NC	0	35	2

ADDRESS
23347

TITLE

Cycloalkyl ketoamides derivatives useful as cathepsin k inhibitors

FILING FEE RECEIVED	FEES: Authority has been given in Paper
1208	No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:

- ☐ All Fees
- ☐ 1.16 Fees (Filing)
- ☐ 1.17 Fees (Processing Ext. of time)
- ☐ 1.18 Fees (Issue)
- ☐ Other _____
- ☐ Credit

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L17           10 SEA ABB=ON  PLU=ON  L12 NOT L7
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                 SEL BABSAN

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L33            7 SEA ABB=ON  PLU=ON  L29 AND 6498996/BABSAN
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L39            3 SEA ABB=ON  PLU=ON  L28 NOT L29

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L42           30 SEA ABB=ON  PLU=ON  L41/COM
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                 E DEATON D/AU
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                E TAVARES F/AU
L47           41 SEA ABB=ON  PLU=ON  ("TAVARES F"/AU OR "TAVARES FRANCIS"/AU OR
                "TAVARES FRANCIS X"/AU OR "TAVARES FRANCIS XAVIER"/AU)
L48            2 SEA ABB=ON  PLU=ON  L44 AND L45 AND L46 AND L47
L49           20 SEA ABB=ON  PLU=ON  (L44 AND (L45 OR L46 OR L47)) OR (L45 AND
                (L46 OR L47)) OR (L46 AND L47)
L50           20 SEA ABB=ON  PLU=ON  (L48 OR L49 OR L5)
L*** DEL      18 S L26 NOT L50
L51           14 SEA ABB=ON  PLU=ON  L50 NOT L26

     FILE 'REGISTRY' ENTERED AT 17:04:17 ON 06 DEC 2006

     FILE 'MEDLINE, EMBASE, BIOSIS, CAOLD' ENTERED AT 17:04:25 ON 06 DEC 2006
L52            0 SEA ABB=ON  PLU=ON  L7

=> file reg
FILE 'REGISTRY' ENTERED AT 17:04:38 ON 06 DEC 2006
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STRUCTURE FILE UPDATES:    5 DEC 2006  HIGHEST RN 914910-45-5
DICTIONARY FILE UPDATES:   5 DEC 2006  HIGHEST RN 914910-45-5

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  conducting SmartSELECT searches.

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http://www.cas.org/ONLINE/UG/regprops.html

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 17:04:40 ON 06 DEC 2006
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FILE COVERS 1907 - 6 Dec 2006  VOL 145 ISS 24
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FILE LAST UPDATED: 5 Dec 2006 (20061205/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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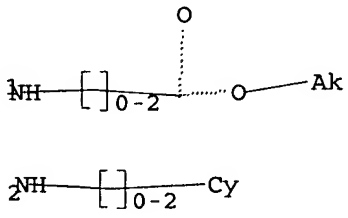
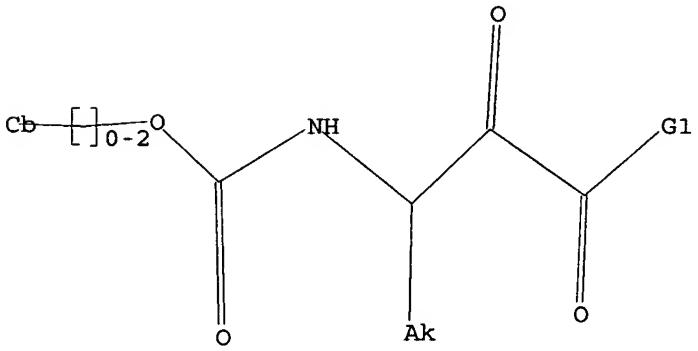
L1 STR





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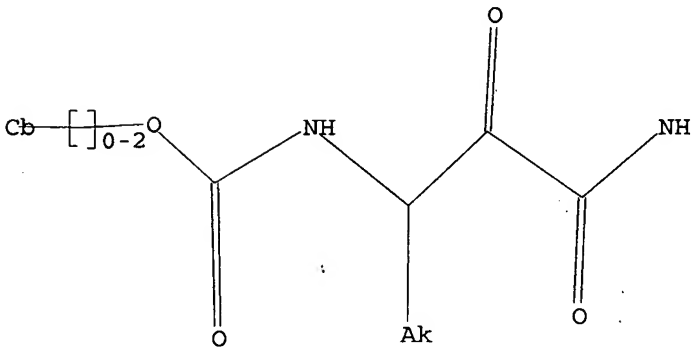
Structure attributes must be viewed using STN Express query preparation.
L2 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2004-501636/AP
L3 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (WO2003-US1271/AP OR WO2003-US 1271/PRN)
L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2002-349812P/PRN
L5 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4)
L6 193 SEA FILE=REGISTRY ABB=ON PLU=ON (103-63-9/BI OR 10445-91-7/BI OR 108-94-1/BI OR 109364-33-2/BI OR 110-91-8/BI OR 1191-95-3/BI OR 120-92-3/BI OR 131403-16-2/BI OR 1450-85-7/BI OR 1462-37-9/BI OR 14924-53-9/BI OR 15159-40-7/BI OR 16269-66-2/BI OR 16640-68-9/BI OR 16889-21-7/BI OR 1722-12-9/BI OR 17452-09-4/BI OR 17452-31-2/BI OR 175203-08-4/BI OR 1820-80-0/BI OR 196934-28-8/BI OR 2015-57-8/BI OR 21754-55-2/BI OR 21872-33-3/BI OR 2389-45-9/BI OR 24255-23-0/BI OR 2627-86-3/BI OR 3034-53-5/BI OR 3099-31-8/BI OR 3731-52-0/BI OR 3779-29-1/BI OR 3844-54-0/BI OR 3884-32-0/BI OR 3886-69-9/BI OR 3934-20-1/BI OR 39608-30-5/BI OR 433219-87-5/BI OR 4415-73-0/BI OR 459-46-1/BI OR 4630-80-2/BI OR 497946-73-3/BI OR 497946-74-4/BI OR 5217-04-9/BI OR 52857-42-8/BI OR 54314-84-0/BI OR 568590-60-3/BI OR 568590-61-4/BI OR 568590-62-5/BI OR 568590-63-6/BI OR

568590-64-7/BI OR 568590-65-8/BI OR 568590-66-9/BI OR 568590-67-0/BI OR 568590-68-1/BI OR 568590-69-2/BI OR 568590-70-5/BI OR 568590-71-6/BI OR 568590-72-7/BI OR 568590-73-8/BI OR 568590-74-9/BI OR 568590-75-0/BI OR 568590-77-2/BI OR 568590-78-3/BI OR 568590-79-4/BI OR 568590-80-7/BI OR 568590-81-8/BI OR 568590-82-9/BI OR 568590-83-0/BI OR 568590-84-1/BI OR 568590-85-2/BI OR 568590-86-3/BI OR 568590-87-4/BI OR 568590-88-5/BI OR 568590-89-6/BI OR 568590-90-9/BI OR 568590-91-0/BI OR 568590-92-1/BI OR 568590-93-2/BI OR 568590-94-3/BI OR 568590-95-4/BI OR 568590-96-5/BI OR 568590-97-6/BI OR 568590-98-7/BI OR 568590-99-8/BI OR 568591-01-5/BI OR 568591-02-6/BI OR 568591-03-7/BI OR 568591-04-8/BI OR 568591-05-9/BI OR 568591-06-0/BI OR 568591-07-1/BI OR 568591-08-2/BI OR 568591-09-3/BI OR 568591-10-6/BI OR 568591-11-7/BI OR 568591-12-8/BI OR 568591-14-0/BI OR 568591-15-1/BI OR 568591-16-2/BI OR 568591-17-3/BI OR 568591-18-4/BI OR 568591-19-5/BI OR 568591-20-8/BI O

L7 98 SEA FILE=REGISTRY SSS FUL L1

L8 38 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND L7

L10 STR



Structure attributes must be viewed using STN Express query preparation.

L12 108 SEA FILE=REGISTRY SSS FUL L10

L13 38 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND L6

L14 38 SEA FILE=REGISTRY ABB=ON PLU=ON (L8 OR L13)

L17 10 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L7

L18 21 SEA FILE=HCAPLUS ABB=ON PLU=ON L7

L19 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L14

L20 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L17

L21 25 SEA FILE=HCAPLUS ABB=ON PLU=ON (L18 OR L19 OR L20)

L22 25 SEA FILE=HCAPLUS ABB=ON PLU=ON (L21 OR L5)

L23 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 NOT L5

L24 25 SEA FILE=HCAPLUS ABB=ON PLU=ON L12

L25 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 NOT L5

L26 24 SEA FILE=HCAPLUS ABB=ON PLU=ON (L23 OR L25)

L44 35 SEA FILE=HCAPLUS ABB=ON PLU=ON ("CATALANO J"/AU OR "CATALANO J G"/AU OR "CATALANO JOHN"/AU OR "CATALANO JOHN G"/AU OR "CATALANO JOHN GEORGE"/AU)

L45 47 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DEATON D"/AU OR "DEATON DAVID"/AU OR "DEATON DAVID N"/AU OR "DEATON DAVID NORMAN"/AU)

L46 545 SEA FILE=HCAPLUS ABB=ON PLU=ON ("MILLER A"/AU OR "MILLER A B"/AU OR "MILLER AARON"/AU OR "MILLER AARON B"/AU OR "MILLER AARON BAYNE"/AU)

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L47          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("TAVARES F"/AU OR "TAVARES
                FRANCIS"/AU OR "TAVARES FRANCIS X"/AU OR "TAVARES FRANCIS
                XAVIER"/AU)
L48           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44 AND L45 AND L46 AND L47
L49          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L44 AND (L45 OR L46 OR L47))
                OR (L45 AND (L46 OR L47)) OR (L46 AND L47)
L50          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L48 OR L49 OR L5)
L51          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 NOT L26

=> d ibib abs l51 tot

L51  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:270628  HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER:          144:285531
TITLE:                    Design of cathepsin K inhibitors for osteoporosis
AUTHOR(S):                Deaton, David N.; Tavares, Francis
                          X.
CORPORATE SOURCE:         Department of Medicinal Chemistry, GlaxoSmithKline,
                          Research Triangle Park, NC, 27709, USA
SOURCE:                   Current Topics in Medicinal Chemistry (Sharjah, United
                          Arab Emirates) (2005), 5(16), 1639-1675
                          CODEN: CTMCCL; ISSN: 1568-0266
PUBLISHER:                Bentham Science Publishers Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB    A review. Osteoporosis is a progressive, debilitating bone disease
      resulting in increased cost and morbidity to the elderly. This review
      summarizes the therapeutic approaches taken in the treatment of
      osteoporosis with particular emphasis on cathepsin K inhibitors.
      Cathepsin K, a cysteine protease predominantly expressed in osteoclasts,
      is a key player involved in bone matrix degradation Both genetic ablation and
      small mol. inhibitor strategies vs. cathepsin K have validated the
      importance of this enzyme in bone resorption. Starting from
      aldehyde-based leads, this review synopsizes the design of improved small
      mol. inhibitors by GlaxoWellcome researchers. These efforts involved the
      evaluation of various warheads, including cyanamides, ketoheterocycles,
      and ketoamides. Initial structure/activity relationships of
      aldehyde-based inhibitors proved useful in the design of ketoamide-based
      cathepsin K inhibitors. Further exploration of S3, S2, S1, and S1·
      subsites with P3, P2, P1, and P1· probes have resulted in the
      identification of potent, selective, orally bioavailable ketoamide-based
      inhibitors of cathepsin K with demonstrated in vivo efficacy.
REFERENCE COUNT:          199   THERE ARE 199 CITED REFERENCES AVAILABLE FOR
                                THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                                FORMAT

L51  ANSWER 2 OF 14  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:128532  HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER:          144:304509
TITLE:                    Novel, potent P2-P3 pyrrolidine derivatives of
                          ketoamide-based cathepsin K inhibitors
AUTHOR(S):                Barrett, David G.; Catalano, John G.;
                          Deaton, David N.; Hassell, Anne M.; Long,
                          Stacey T.; Miller, Aaron B.; Miller, Larry
                          R.; Ray, John A.; Samano, Vicente; Shewchuk, Lisa M.;
                          Wells-Knecht, Kevin J.; Willard, Derril H.; Wright,
                          Lois L.
CORPORATE SOURCE:         Department of Medicinal Chemistry, GlaxoSmithKline,
```

Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(6), 1735-1739
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:304509
AB Starting from a potent pantolactone ketoamide cathepsin K inhibitor discovered from structural screening, conversion of the lactone scaffold to a pyrrolidine scaffold allowed exploration of the S3 subsite of cathepsin K. Manipulation of P3 and P1' groups afforded potent inhibitors with drug-like properties.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:16634 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 144:184023
TITLE: Semicarbazone-based inhibitors of cathepsin K, are they prodrugs for aldehyde inhibitors?
AUTHOR(S): Adkison, Kim K.; Barrett, David G.; ***Deaton, David N.***; Gampe, Robert T.; Hassell, Anne M.; Long, Stacey T.; McFadyen, Robert B.; ***Miller, Aaron B.***; Miller, Larry R.; Payne, J. Alan; Shewchuk, Lisa M.; Wells-Knecht, Kevin J.; Willard, Derril H.; Wright, Lois L.
CORPORATE SOURCE: Department of Research Bioanalysis and Drug Metabolism, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorg. Med. Chem. Lett. (2006), 16(4), 978-983
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Starting from potent aldehyde inhibitors with poor drug properties, derivatization to semicarbazones led to the identification of a series of semicarbazone-based cathepsin K inhibitors with greater solubility and better pharmacokinetic profiles than their parent aldehydes. Furthermore, a representative semicarbazone inhibitor attenuated bone resorption in an ex vivo rat calvarial bone resorption model. However, based on enzyme inhibition comparisons at neutral pH, semicarbazone hydrolysis rates, and 13C NMR expts., these semicarbazones probably function as prodrugs of aldehydes.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:708480 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 143:347441
TITLE: Ketoheterocycle-based inhibitors of cathepsin K: A novel entry into the synthesis of peptidic ketoheterocycles
AUTHOR(S): ***Tavares, Francis X.***; ***Deaton, David N.***; ***Miller, Aaron B.***; Miller, Larry R.; Wright, Lois L.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005),

15(17), 3891-3895
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:347441

AB Ketoheterocyclic inhibitors of cathepsin K have been disclosed. SAR of potency enhancing P2-P3 groups coupled with ketoheterocyclic warheads to provide cathepsin K inhibitors have been described. In addition, a novel route to access α-ketothiazoles using a key thioamide functionality has been disclosed. The mild method employed allows for the presence of diverse functional groups, such as amide and carbamate functionalities, commonly found in protease inhibitors that have peptidomimetic scaffolds. This new method should provide a quick entry into functionally diverse protease inhibitors.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

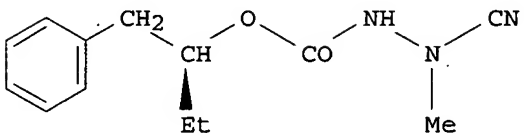
L51 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:589354 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 143:259481
TITLE: P2-P3 conformationally constrained ketoamide-based inhibitors of cathepsin K
AUTHOR(S): Barrett, David G.; Boncek, Virginia M.; ***Catalano, John G.***; ***Deaton, David N.***; Hassell, Anne M.; Jurgensen, Cynthia H.; Long, Stacey T.; McFadyen, Robert B.; ***Miller, Aaron B.***; Miller, Larry R.; Payne, J. Alan; Ray, John A.; Samano, Vicente; Shewchuk, Lisa M.; ***Tavares, Francis X.***; Wells-Knecht, Kevin J.; Willard, Derril H.; Wright, Lois L.; Zhou, Hui-Qiang Q.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(15), 3540-3546
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:259481

AB An orally bioavailable series of ketoamide-based cathepsin K inhibitors with good pharmacokinetic properties has been identified. Starting from a potent inhibitor endowed with poor drug properties, conformational constraint of the P2-P3 linker and modifications to P 1 ' elements led to an enhancement in potency, solubility, clearance, and bioavailability. These optimized inhibitors attenuated bone resorption in a rat TPTX hypocalcemic bone resorption model.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:511371 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 143:165992
TITLE: Acyclic cyanamide-based inhibitors of cathepsin K
AUTHOR(S): Barrett, David G.; ***Deaton, David N.***; Hassell, Anne M.; McFadyen, Robert B.; ***Miller, Aaron B.***; Miller, Larry R.; Payne, J. Alan; Shewchuk, Lisa M.; Willard, Derril H., Jr.; Wright, Lois L.

CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(12), 3039-3043
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:165992
GI



I

AB Conversion of the proline-derived cyanamide lead to an acyclic cyanamide capable of forming an addnl. hydrogen bond with cathepsin K resulted in a large increase in inhibitory activity. An X-ray structure of a co-crystal of a cyanamide with cathepsin K confirmed the enzyme interaction. Furthermore, a representative acyclic cyanamide inhibitor I was able to attenuate bone resorption in the rat calvarial model.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:244461 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 142:441287
TITLE: Novel and potent cyclic cyanamide-based cathepsin K inhibitors
AUTHOR(S): ***Deaton, David N.***; Hassell, Anne M.; McFadyen, Robert B.; ***Miller, Aaron B.***; Miller, Larry R.; Shewchuk, Lisa M.; ***Tavares, Francis X.***; Willard, Derril H.; Wright, Lois L.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(7), 1815-1819
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:441287
AB Starting from a PDE IV inhibitor hit derived from high throughput screening of the compound collection, a key pyrrolidine cyanamide pharmacophore was identified. Modifications of the pyrrolidine ring produced enhancements in cathepsin K inhibition. An X-ray co-crystal

structure of a cyanamide with cathepsin K confirmed the mode of inhibition.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:465485 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 141:191052
TITLE: Exploration of the P2-P3 SAR of aldehyde cathepsin K inhibitors
AUTHOR(S): Boros, Eric E.; ***Deaton, David N.***; Hassell, Anne M.; McFadyen, Robert B.; ***Miller, Aaron B.***; Miller, Larry R.; Paulick, Margot G.; Shewchuk, Lisa M.; Thompson, James B.; Willard, Derril H.; Wright, Lois L.
CORPORATE SOURCE: GlaxoSmithKline, Department of Medicinal Chemistry, Research Triangle Park, NC, 27709-3398, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(13), 3425-3429
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:191052
AB The synthesis via peptide coupling and oxidation and biol. activity of a series of aldehyde inhibitors of cathepsin K are reported. Exploration of the properties of the S2 and S3 subsites with a series of carbamate derivatized norleucine aldehydes substituted at the P2 and P3 positions afforded analogs with cathepsin K IC50s between 600 nM and 130 pM.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:346257 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 141:81691
TITLE: Orally bioavailable small molecule ketoamide-based inhibitors of cathepsin K
AUTHOR(S): Barrett, David G.; ***Catalano, John G.***; ***Deaton, David N.***; Long, Stacey T.; Miller, Larry R.; ***Tavares, Francis X.***; Wells-Knecht, Kevin J.; Wright, Lois L.; Zhou, Hui-Qiang Q.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(10), 2543-2546
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:81691
AB An orally available series of ketoamide-based inhibitors of cathepsin K has been identified. Starting from a potent inhibitor with poor oral bioavailability, modifications to P1 and P1' elements led to enhancements in solubility and permeability. These improvements resulted in orally available cathepsin K inhibitors.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:1001233 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 140:192214
TITLE: Design of Potent, Selective, and Orally Bioavailable Inhibitors of Cysteine Protease Cathepsin K
AUTHOR(S): ***Tavares, Francis X.***; Boncek, Virginia; ***Deaton, David N.***; Hassell, Anne M.; Long, Stacey T.; ***Miller, Aaron B.***; Payne, Alan A.; Miller, Larry R.; Shewchuk, Lisa M.; Wells-Knecht, Kevin; Willard, Derril H., Jr.; Wright, Lois L.; Zhou, Hui-Qiang
CORPORATE SOURCE: Department of Medicinal Chemistry, Discovery Research Biology, Department of Research Bioanalysis and Drug Metabolism, Discovery Research CASS Department of Molecular Pharmacology Preclinical Development and Department of Gene Expression and Protein Biochemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(3), 588-599
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:192214

AB Osteoclast-mediated bone matrix resorption has been attributed to cathepsin K, a cysteine protease of the papain family that is abundantly and selectively expressed in osteoclast. Inhibition of cathepsin K could potentially be an effective method to prevent osteoporosis. Structure-activity studies on a series of reversible ketoamides based inhibitors of cathepsin K have led to identification of potent and selective compds. Crystallog. studies have given insights into the mode of binding of these inhibitors. A series of ketoamides with varying P1 moieties were first synthesized to find an optimum group that would fit into the S1 subsite of the cysteine protease, cathepsin K. With a desired P1 group in place a variety of heterocyclic analogs in the P' region were synthesized to study their steric and electronic effects. In the process of exploring these P' heterocyclic variations, excellent selectivity was gained over other highly homologous cysteine proteases, including cathepsins L, S, and V. The favorable pharmacokinetic properties of some of these cathepsin K inhibitors in rats make them suitable for evaluation in rodent osteoporosis models. A representative cathepsin K inhibitor was shown to attenuate PTH-stimulated hypercalcemia in the TPTX rat model. These inhibitors provide a viable lead series in the discovery of new therapies for the prevention and treatment of osteoporosis.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:981492 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 140:217361
TITLE: Exploration of the P1 SAR of aldehyde cathepsin K inhibitors
AUTHOR(S): ***Catalano, John G.***; ***Deaton, David N.***; Furfine, Eric S.; Hassell, Annie M.; McFadyen, Robert B.; ***Miller, Aaron B.***; Miller, Larry R.; Shewchuk, Lisa M.; Willard, Derril H.; Wright, Lois L.
CORPORATE SOURCE: GlaxoSmithKline, Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709-3398, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(1), 275-278
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:217361

AB The synthesis and biol. activity of a series of (formylalkyl)carbamic acid dimethylethyl esters (amino aldehyde) inhibitors of cathepsin K are reported. Exploration of the properties of the S1 subsite with a series of α-amino aldehyde derivs. substituted at the P1 position afforded compds. with cathepsin K IC50s between 52 μM and 15 nM. The crystal and mol. structures of [(1S)-(cyclohexyl)(formyl)methyl]carbamic acid 1,1-dimethylethyl ester-cathepsin K complex were reported.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:836840 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 139:338188
TITLE: Preparation of 1-(oxoaminoacetyl)pentylcarbamate derivatives as cathepsin K inhibitors for the treatment of bone loss
INVENTOR(S): Barrett, David Gene; ***Catalano, John G.***; ***Deaton, David Norman***; ***Miller, Aaron Bayne***; Ray, John A.; Samano, Vicente
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 183 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086385	A1	20031023	WO 2003-US9893	20030401
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2003262140	A1	20031027	AU 2003-262140	20030401
EP 1494663	A1	20050112	EP 2003-746570	20030401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005532290	T2	20051027	JP 2003-583404	20030401
US 2005245596	A1	20051103	US 2004-510469	20041007
PRIORITY APPLN. INFO.:			US 2002-371524P P	20020410
			WO 2003-US9893 W	20030401

OTHER SOURCE(S): MARPAT 139:338188

AB Heterocycle-substituted ketoamide derivs. A-D-CONHCH[(CH2)4R]COCONH-Z [A is a group Q4p-Q3n-Q2m-Q1-, where Q1 is heterocyclyl or heterocyclylene, Q2 is O2C, CO, NHCO, CONHCO, SO2NHCO, SO2, or NHSO2, Q3 is C1-C6 alkyl,

haloalkyl, C3-C7 cycloalkyl, aralkyl, aralkylene, aryl, arylene, heteroaryl, heteroarylene, heterocyclyl, or heterocyclylene, Q4 is alkyl, haloalkyl, aryl, aryloxy, heteroaryl, halo, or cyano, m, n = 0 or 1 and p is 0-2; D is O or S; R is H or -NR1-R2-R3, where R1, R3 are H or alkyl, R2 is CO, CO2, CONH, SO2, or SO2NH; Z is a group -Xm-X1, where X is CR'R'' (R', R'' are H or alkyl), m = 0-2 and X1 is aryl, heteroaryl, or heterocyclyl] were prepared for use as cathepsin K inhibitors. Compds. of the invention are used in the manufacture of medicaments for the treatment of disorders, including osteoporosis, associated with an imbalance between bone resorption and formation which can ultimately lead to fracture. Thus, (3S)-4,4-dimethyl-1-[[4-(trifluoromethyl)anilino]carbonyl]pyrrolidinyl (1S)-1-[oxo(1H-pyrazol-5-ylamino)acetyl]pentylcarbamate, prepared by a multistep procedure, showed IC50 in the range 1-0.1 nM for inhibition of cathepsin K.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:591140 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 139:133839
TITLE: Preparation of cycloalkyl α-ketoamide derivatives as cathepsin K inhibitors
INVENTOR(S): ***Catalano; John George; Deaton, David Norman; Miller, Aaron Bayne; Tavares, Francis Xavier***
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2003062192	A1	20030731	WO 2003-US1271		20030115	<--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
EP 1465862	A1	20041013	EP 2003-703836		20030115	<--
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JP 2005515254	T2	20050526	JP 2003-562076		20030115	<--
US 2005054819	A1	20050310	US 2004-501636		20040715	<--
PRIORITY APPLN. INFO.:			US 2002-349812P	P	20020117	<--
			WO 2003-US1271	W	20030115	<--

OTHER SOURCE(S): MARPAT 139:133839
AB Cycloalkyl ketoamide derivs. A-O2CNHCH(D)COCONH-Z [A is the group Q3-Q2-Q1-(CH2)0-2, where Q1 is cycloalkylene, Q2 is null, alkylene (R), OR, SR, NRR' (R' = H, alkyl); Q3 is (un)substituted (hetero)aryl; D is alkyl or amino group-substituted alkyl; Z is the group -X0-2-X10-1-X2, where X is (alkyl)methylene, X1 is CO2CH2, and X2 is (hetero)aryl or

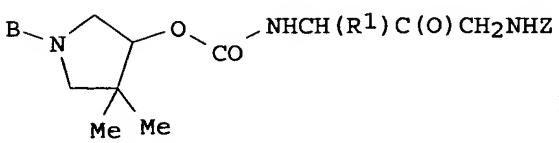
heterocyclyl] were prepared for use as cathepsin K inhibitors in the treatment of disorders, including osteoporosis, associated with enhanced bone turnover which can ultimately lead to fracture. Thus, [1-(4-fluorobenzyl)cyclobutyl]methyl (1S)-1-[oxo(1H-pyrazol-5-ylamino)acetyl]pentylcarbamate was prepared by phosgenation of [1-(4-fluorobenzyl)cyclobutyl]methanol, coupling with Me (2S)-2-aminohexanoate, treatment of the ester with (triphenylphosphoranylidene)acetonitrile, and reaction with 3-aminopyrazole. The product showed Ki < 1 nM for inhibition of cathepsin K.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:301078 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 138:304173
TITLE: Preparation of pyridinylsulfonylamino-containing keto carbamates as inhibitors of cathepsin K useful against osteoporosis and other disorders
INVENTOR(S): ***Deaton, David Norman; Catalano, John George***
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003031437	A1	20030417	WO 2002-US31480		20021002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1448554	A1	20040825	EP 2002-800886		20021002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005537216	T2	20051208	JP 2003-534420		20021002
US 2005043368	A1	20050224	US 2004-492059		20040408
PRIORITY APPLN. INFO.:			US 2001-327938P	P	20011009
			WO 2002-US31480	W	20021002

OTHER SOURCE(S): MARPAT 138:304173
GI

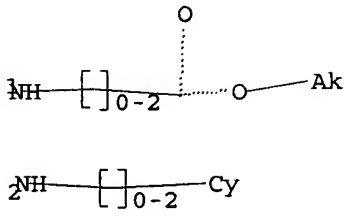


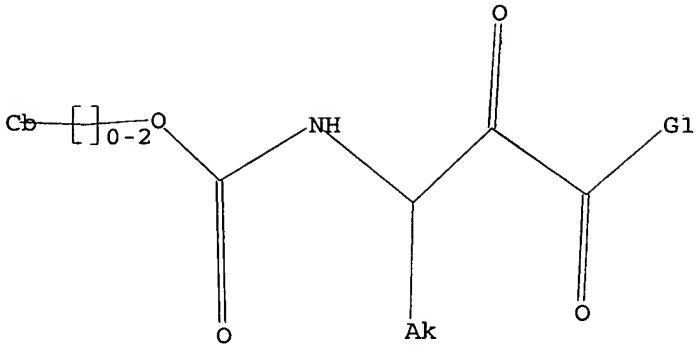
I

AB The present invention includes pyridinylsulfonylamino-containing keto carbamates (ACH(R1)DC(O)NHCH(R2)C(O)CH2NHZ (I) and II; variables defined below; e.g. (1S)-2,2-dimethyl-1-[[3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]methyl]propyl 2-oxo-3-[(2-pyridinylsulfonyl)amino]propylcarbamate), which are useful as cathepsin K inhibitors. The described invention also includes methods of making such ketone derivs. as well as methods of using the same in the treatment of disorders, including osteoporosis. Although the methods of preparation are not claimed, 19 example prepns. are included. Each of the compds. exemplified in the Examples section bind with high affinity (IC50 < 10 μM) to the cathepsin K enzyme, e.g. (1S)-1-[[4-(1H-imidazol-1-yl)phenoxy]methyl]-2,2-dimethylpropyl (1S)-1-[[(2-pyridinylsulfonyl)amino]acetyl]pentylcarbamate exhibits an IC50 of .apprx.10-1 nM or less. For I: A = (Q3)p-(Q2)n -(Q1)-(Q)m- (Q is CH2 and m = 0-2, or Q is OCH2 and m is 1, or Q is N(R3)CH2 and m is 1, where R3 is H or C1-C6 alkyl; Q1 is aryl, heteroaryl, or heterocyclyl; Q2 is CH2 and n is 0 or 1, or Q2 is O and n is 1, or Q2 is N(R3) and n is 1, where R3 is H or C1-C6 alkyl; Q3 is aryl or heteroaryl and p is 0 or 1). R1 is alkyl or cycloalkyl, said cycloalkyl may be optionally substituted with alkyl; D is O or S; R2 is H or alkyl; and Z is -(X1)q-(X2) (X1 is S(O)2, C(O), or -CH2-, and q = 0-2; and X2 is aryl, heteroaryl, or heterocyclyl). For II: B is -(Q1)a-(Q2)b-(Q3) (Q1 is C(O), S(O)2, or CR2R3, where R2 and R3 each = H or C1-C6 alkyl, and a = 0-3; Q2 is O, S, NR2, or CR2R3, where R2 and R3 each = H or C1-C6 alkyl, and b = 0-3; and Q3 is aryl, heteroaryl, heterocyclyl, aralkyl, or alkyleneheterocyclyl). R1 is H or alkyl; Z is -(X1)q-(X2) (X1 is S(O)2, C(O), or alkyl, and q is 0 or 1; and X2 is aryl, heteroaryl, or heterocyclyl).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d que l26
L1 STR





G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

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L3 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (WO2003-US1271/AP OR WO2003-US 1271/PRN)

L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2002-349812P/PRN

L5 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4)

L6 193 SEA FILE=REGISTRY ABB=ON PLU=ON (103-63-9/BI OR 10445-91-7/BI OR 108-94-1/BI OR 109364-33-2/BI OR 110-91-8/BI OR 1191-95-3/BI OR 120-92-3/BI OR 131403-16-2/BI OR 1450-85-7/BI OR 1462-37-9/BI OR 14924-53-9/BI OR 15159-40-7/BI OR 16269-66-2/BI OR 16640-68-9/BI OR 16889-21-7/BI OR 1722-12-9/BI OR 17452-09-4/BI OR 17452-31-2/BI OR 175203-08-4/BI OR 1820-80-0/BI OR 196934-28-8/BI OR 2015-57-8/BI OR 21754-55-2/BI OR 21872-33-3/BI OR 2389-45-9/BI OR 24255-23-0/BI OR 2627-86-3/BI OR 3034-53-5/BI OR 3099-31-8/BI OR 3731-52-0/BI OR 3779-29-1/BI OR 3844-54-0/BI OR 3884-32-0/BI OR 3886-69-9/BI OR 3934-20-1/BI OR 39608-30-5/BI OR 433219-87-5/BI OR 4415-73-0/BI OR 459-46-1/BI OR 4630-80-2/BI OR 497946-73-3/BI OR 497946-74-4/BI OR 5217-04-9/BI OR 52857-42-8/BI OR 54314-84-0/BI OR 568590-60-3/BI OR 568590-61-4/BI OR 568590-62-5/BI OR 568590-63-6/BI OR 568590-64-7/BI OR 568590-65-8/BI OR 568590-66-9/BI OR 568590-67-0/BI OR 568590-68-1/BI OR 568590-69-2/BI OR 568590-70-5/BI OR 568590-71-6/BI OR 568590-72-7/BI OR 568590-73-8/BI OR 568590-74-9/BI OR 568590-75-0/BI OR 568590-77-2/BI OR 568590-78-3/BI OR 568590-79-4/BI OR 568590-80-7/BI OR 568590-81-8/BI OR 568590-82-9/BI OR 568590-83-0/BI OR 568590-84-1/BI OR 568590-85-2/BI OR 568590-86-3/BI OR 568590-87-4/BI OR 568590-88-5/BI OR 568590-89-6/BI OR 568590-90-9/BI OR 568590-91-0/BI OR 568590-92-1/BI OR 568590-93-2/BI OR 568590-94-3/BI OR 568590-95-4/BI OR 568590-96-5/BI OR 568590-97-6/BI OR 568590-98-7/BI OR 568590-99-8/BI OR

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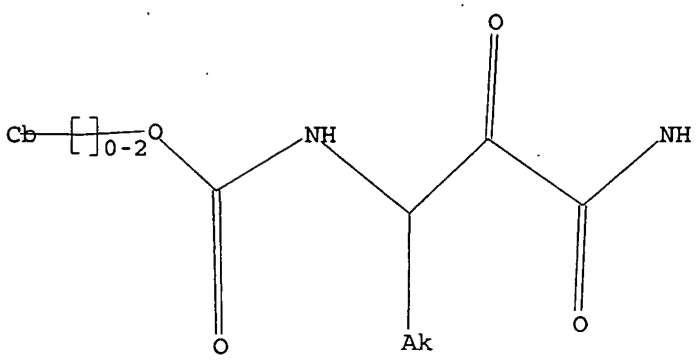
L7 98 SEA FILE=REGISTRY SSS FUL L1
L8 38 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND L7
L10 STR



Structure attributes must be viewed using STN Express query preparation.

L12 108 SEA FILE=REGISTRY SSS FUL L10
L13 38 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND L6
L14 38 SEA FILE=REGISTRY ABB=ON PLU=ON (L8 OR L13)
L17 10 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L7
L18 21 SEA FILE=HCAPLUS ABB=ON PLU=ON L7
L19 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L14
L20 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L21 25 SEA FILE=HCAPLUS ABB=ON PLU=ON (L18 OR L19 OR L20)
L22 25 SEA FILE=HCAPLUS ABB=ON PLU=ON (L21 OR L5)
L23 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 NOT L5
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=> d ibib abs hitstr retable l26 tot

L26 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:331910 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 143:52911
TITLE: A structural screening approach to ketoamide-based inhibitors of cathepsin K
AUTHOR(S): Barrett, David G.; Catalano, John G.; Deaton, David N.; Long, Stacey T.; McFadyen, Robert B.; Miller, Aaron B.; Miller, Larry R.; Wells-Knecht, Kevin J.; Wright, Lois L.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(9), 2209-2213
CODEN: BMCLE8; ISSN: 0960-894X

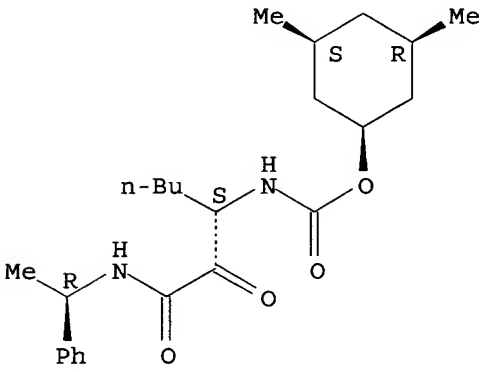
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:52911

AB Several novel ketoamide-based inhibitors of cathepsin K have been identified. Starting from a modestly potent inhibitor, structural screening of P2 elements led to 100-fold enhancements in inhibitory activity. Modifications to one of these leads resulted in an orally bioavailable cathepsin K inhibitor.

IT ***854001-49-3P 854001-50-6P 854001-51-7P 854001-52-8P 854001-53-9P 854001-54-0P 854494-51-2P***
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structural screening approach to ketoamide-based inhibitors of cathepsin K)

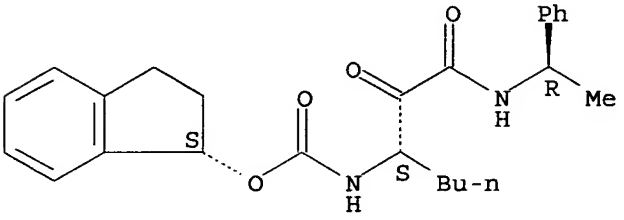
RN 854001-49-3 HCAPLUS
CN Carbamic acid, [1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1α,3α,5α)-3,5-dimethylcyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 854001-50-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1S)-2,3-dihydro-1H-inden-1-yl ester (9CI) (CA INDEX NAME)

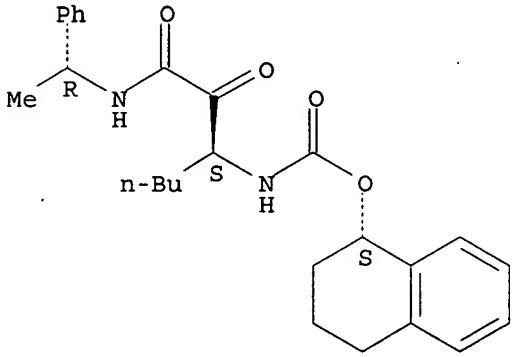
Absolute stereochemistry.



RN 854001-51-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-,

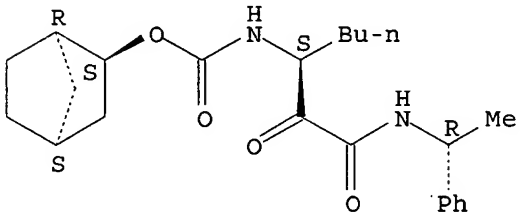
(1S)-1,2,3,4-tetrahydro-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



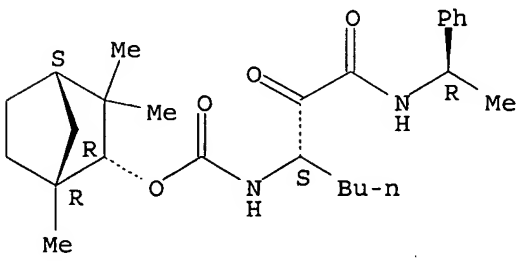
RN 854001-52-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1R,2S,4S)-bicyclo[2.2.1]hept-2-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



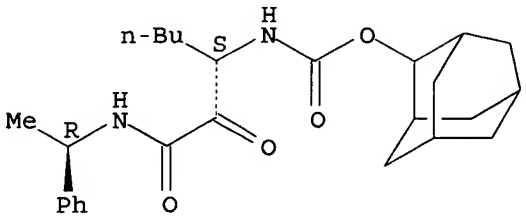
RN 854001-53-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1R,2R,4S)-1,3,3-trimethylbicyclo[2.2.1]hept-2-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



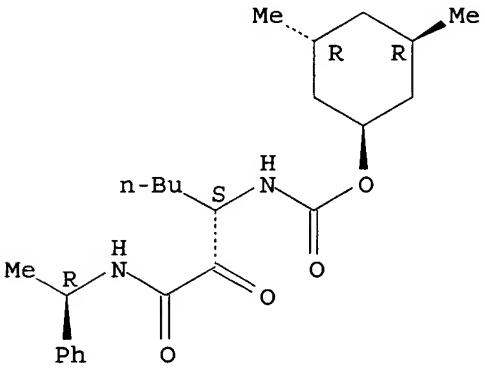
RN 854001-54-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, tricyclo[3.3.1.13,7]dec-2-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 854494-51-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (3R,5R)-3,5-dimethylcyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

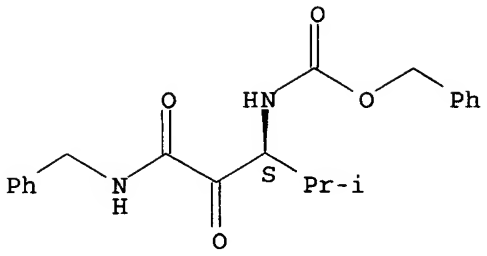
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Barril, X	2004	4	779	Mini-Rev Med Chem	HCAPLUS
Boros, E	2004	14	3425	Bioorg Med Chem Lett	HCAPLUS
Catalano, J	2004	14	275	Bioorg Med Chem Lett	HCAPLUS
Catalano, J	2004	14	719	Bioorg Med Chem Lett	HCAPLUS
Deaton, D	2004	42	245	Prog Med Chem	HCAPLUS
Dressman, J	1998	15	11	Pharm Res	HCAPLUS
Einhorn, T	1996		3	Osteoporosis	
Gelb, B	1996	273	1236	Science	HCAPLUS
Kiviranta, R	2005	36	159	Bone	HCAPLUS
Kopelevich, V	1979		3893	Tetrahedron Lett	HCAPLUS
Lambert, M	1997		243	Practical Applicatio	HCAPLUS
Li, Z	2002	277	28669	J Biol Chem	HCAPLUS
Marquis, R	2001	44	1380	J Med Chem	HCAPLUS
McGrath, M	1997	4	105	Nat Struct Biol	HCAPLUS
Somoza, J	2002	322	559	J Mol Biol	HCAPLUS
Stroup, G	2001	16	1739	J Bone Miner Res	HCAPLUS
Tavares, F	2004	47	588	J Med Chem	HCAPLUS
Vaaraniemi, J	2004	19	1432	J Bone Miner Res	HCAPLUS
Wasserman, H	1997	38	953	Tetrahedron Lett	HCAPLUS

L26 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:150046 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 142:392651
TITLE: Development of α-keto-based inhibitors of cruzain, a cysteine protease implicated in Chagas disease
AUTHOR(S): Choe, Youngchool; Brinen, Linda S.; Price, Mark S.; Engel, Juan C.; Lange, Meinolf; Grisostomi, Corinna; Weston, Scott G.; Pallai, Peter V.; Cheng, Hong; Hardy, Larry W.; Hartsough, David S.; McMakin, Marsha; Tilton, Robert F.; Baldino, Carmen M.; Craik, Charles S.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of California at San Francisco, San Francisco, CA, 94143-2280, USA
SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(6), 2141-2156
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:392651

AB Trypanosoma cruzi, a protozoan parasite, is the causative agent of Chagas disease, a major cause of cardiovascular disease in many Latin American countries. There is an urgent need to develop an improved therapy due to the toxicity of existing drugs and emerging drug resistance. Cruzain, the primary cysteine protease of T. cruzi, is essential for the survival of the parasite in host cells and therefore is an important target for the development of inhibitors as potential therapeutics. A novel series of α-ketoamide-, α-keto acid-, α-keto ester-, and aldehyde-based inhibitors of cruzain has been developed. The inhibitors were identified by screening protease targeted small mol. libraries and systematically optimizing the P1, P2, P3, and P1' residues using specific structure-guided methods. A total of 20 compds. displayed picomolar potency in in vitro assays and three inhibitors representing different α-keto-based inhibitor scaffolds demonstrated anti-trypanosomal activity in cell culture. A 2.3 Å crystallog. structure of cruzain bound with one of the α-ketoester analogs is also reported. The structure and kinetic assay data illustrate the covalent binding, reversible inhibition mechanism of the inhibitor. Information on the compds. reported here will be useful in the development of new lead compds. as potential therapeutic agents for the treatment of Chagas disease and as biol. probes to study the role that cruzain plays in the pathol. This study also demonstrates the validity of structure-guided approaches to focused library design and lead compound optimization.

IT ***869277-18-9P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(peptidyl α-keto-based inhibitors of cruzain, a cysteine protease implicated in chagas disease)
RN 869277-18-9 HCAPLUS
CN Carbamic acid, [(1S)-1-(1-methylethyl)-2,3-dioxo-3-[(phenylmethyl)amino]propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Almquist, R	1980	23	1392	J Med Chem	HCAPLUS
Angelastro, M	1990	33	11	J Med Chem	HCAPLUS
Anon				World Health Organiz	
Baldino, C	2004		15	Curr Drug Discov	
Baldino, C	2000	2	89	J Comb Chem	HCAPLUS
Baldino, C	2000			US Patent	
Brinen, L	2000	8	831	Struct Fold Des	HCAPLUS
Cleland, W	1979	103		Methods in Enzymolog	
Coffen, D	1998	8	206	Med Chem Res	HCAPLUS
Du, X	2000	7	733	Chem Biol	HCAPLUS
Du, X	2002	45	2695	J Med Chem	HCAPLUS
Eakin, A	1992	267	7411	J Biol Chem	HCAPLUS
Eakin, A	1993	268	6115	J Biol Chem	HCAPLUS
Eggers, C	2001	308	975	J Mol Biol	HCAPLUS
Engel, J	1998	111	597	J Cell Sci	
Engel, J	1998	188	725	J Exp Med	HCAPLUS
Gerber, P	1995	9	251	J Comput Aided Mol D	HCAPLUS
Gillmor, S	1997	6	1603	Protein Sci	HCAPLUS
Harbeson, S	1994	37	2918	J Med Chem	HCAPLUS
Hu, L	1990	281	271	Arch Biochem Biophys	HCAPLUS
Itow, S	1977	24	591	J Protozool	HCAPLUS
LaLonde, J	1998	41	4567	J Med Chem	HCAPLUS
Li, Z	1993	36	3472	J Med Chem	HCAPLUS
Li, Z	1996	39	4089	J Med Chem	HCAPLUS
McGrath, M	1995	247	251	J Mol Biol	HCAPLUS
Navaza, J	1994	50	157	Acta Crystallogr	
Otwinowski, Z	1993			Proceedings of the C	
Potterton, E	2003	D59	1131	Acta Crystallogr	HCAPLUS
Reetz, M	1996		335	Liebigs Ann	HCAPLUS
Roush, W	1998	8	2809	Bioorg Med Chem Lett	HCAPLUS
Rutenber, E	1996	4	1545	Bioorg Med Chem	HCAPLUS
Sack, J	1988	6	244	J Mol Graphics	
Sasaki, T	1990	3	195	J Enzyme Inhib	HCAPLUS
Scheidt, K	1998	6	2477	Bioorg Med Chem	HCAPLUS
Shoichet, B	1993	6	723	Protein Eng	HCAPLUS
Szelke, M	1982	299	555	Nature	HCAPLUS
Thompson, S	1998	41	3923	J Med Chem	HCAPLUS
Walter, J	1983	364	949	Hoppe Seylers Z Phys	HCAPLUS
Wassermann, H	1997	38	953	Tetrahedron Lett	

L26 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1154671 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 142:94135

TITLE: Process and intermediates for the preparation of (1R,2S,5S)-N-[3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-3-[(2S)-2-[[[[1,1-dimethylethyl]amino]carbonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide

INVENTOR(S): Sudhakar, Anantha; Dahanukar, Vilas; Zavialov, Ilia A.; Orr, Cecilia; Nguyen, Hoa N.; Weber, Juergen; Jeon, Ingyu; Chen, Minzhang; Green, Michael D.; Wong, George S.; Park, Jeonghan; Iwama, Tetsuo

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113294	A1	20041229	WO 2004-US18914	20040615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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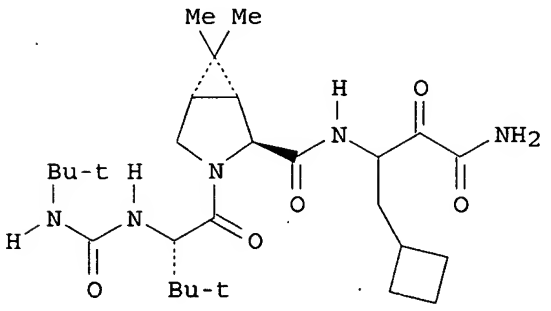
CA 2526629	AA	20041229	CA 2004-2526629	20040615
US 2005059800	A1	20050317	US 2004-867600	20040615
EP 1641754	A1	20060405	EP 2004-755225	20040615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1805932	A	20060719	CN 2004-80016640	20040615

PRIORITY APPLN. INFO.:
US 2003-479517P P 20030617
WO 2004-US18914 W 20040615

OTHER SOURCE(S): CASREACT 142:94135; MARPAT 142:94135

GI

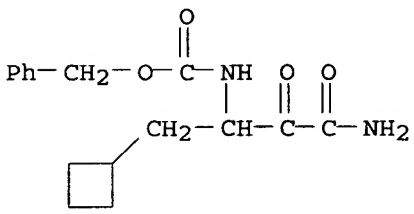


I

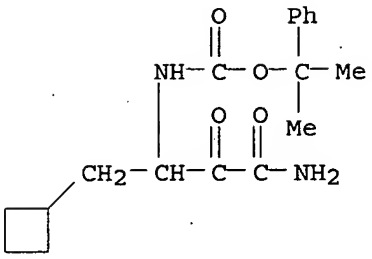
AB In one embodiment, the present application relates to a process of making a compound of formula (I) and to certain intermediate compds. that are made within the process of making the compound I. I is an inhibitor of hepatitis C virus NS3/NS4a serine protease. Thus, (2S)-2-(tert-butylaminocarbonylamino)-3,3-dimethylbutanoic acid was condensed with Me (1R,2S,5S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxylate hydrochloride using EDCI, HOBt, and 2,6-lutidine in MeCN followed by hydrolysis with 10% aqueous LiOH and acidification with 3 N aqueous HCl and treatment with L-α-methylbenzylamine to give (1R,2S,5S)-3-[(2S)-2-[[[[1,1-dimethylethyl]amino]carbonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxylic acid (II) L-α-methylbenzylamine salt which was treated with a mixture of 1 N aqueous HCl and Me tert-Bu ether to give free acid II. 4-(Tert-butoxycarbonylamino)-4-cyclobutyl-2-hydroxybutanamide was oxidized by DMSO, EDCI, and Cl2CHCO2H in isopropanol to give 4-(tert-butoxycarbonylamino)-4-cyclobutyl-2-oxobutanamide which was treated with HCl in isopropanol to give 4-amino-4-cyclobutyl-2-oxobutanamide hydrochloride which was condensed with II using iso-Bu chloroformate and N-methylmorpholine in EtOAc to give I.

IT ***817169-94-1P***, 3-Benzyloxycarbonylamino-4-cyclobutyl-2-oxobutanamide ***817170-14-2P***, 4-Cyclobutyl-3-[[(1-methyl-1-phenylethoxy)carbonyl]amino]-2-oxobutanamide ***817170-16-4P***, 4-Cyclobutyl-3-(cyclobutyloxycarbonylamino)-2-oxobutanamide ***817170-18-6P***, 4-Cyclobutyl-3-[[[(1-methylcyclobutyl)oxy]carbonyl]amino]-2-oxobutanamide ***817170-20-0P***, 3-(Adamantyloxycarbonylamino)-4-cyclobutyl-2-oxobutanamide ***817170-30-2P***, 3-(9-Anthrylmethoxycarbonylamino)-4-cyclobutyl-2-oxobutanamide ***817170-32-4P***, 3-(Diphenylmethoxycarbonylamino)-4-cyclobutyl-2-oxobutanamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process and intermediates for preparation of (1R,2S,5S)-N-[3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-3-[(2S)-2-[[[[1,1-dimethylethyl]amino]carbonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide)

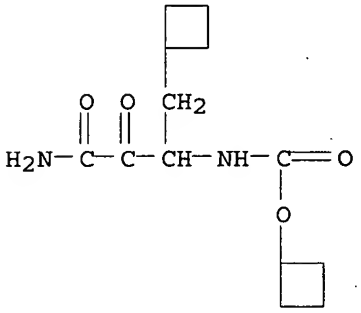
RN 817169-94-1 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



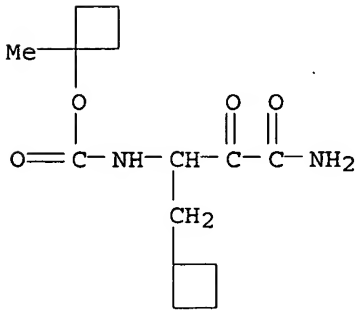
RN 817170-14-2 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, 1-methyl-1-phenylethyl ester (9CI) (CA INDEX NAME)



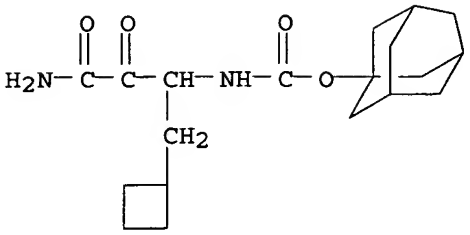
RN 817170-16-4 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, cyclobutyl ester (9CI) (CA INDEX NAME)



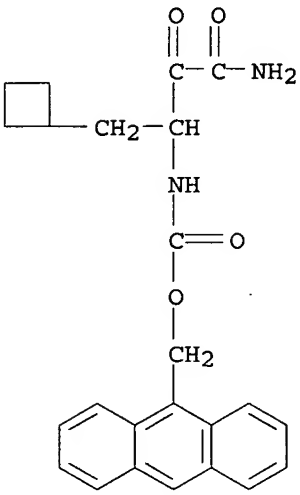
RN 817170-18-6 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, 1-methylcyclobutyl ester (9CI) (CA INDEX NAME)



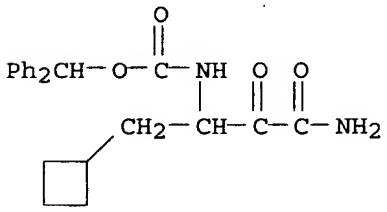
RN 817170-20-0 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, tricyclo[3.3.1.13,7]dec-1-yl ester (9CI) (CA INDEX NAME)



RN 817170-30-2 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, 9-anthracenylmethyl ester (9CI) (CA INDEX NAME)



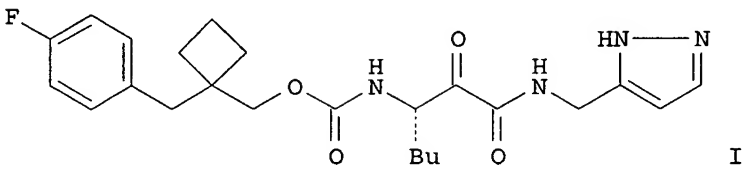
RN 817170-32-4 HCAPLUS
CN Carbamic acid, [3-amino-1-(cyclobutylmethyl)-2,3-dioxopropyl]-, diphenylmethyl ester (9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Schering Corp	2002			WO 0208244 A	HCAPLUS

L26 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:729844 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 141:379687
TITLE: Potent and selective P2-P3 ketoamide inhibitors of cathepsin K with good pharmacokinetic properties via favorable P1', P1, and/or P3 substitutions
AUTHOR(S): Barrett, David G.; Catalano, John G.; Deaton, David N.; Hassell, Anne M.; Long, Stacey T.; Miller, Aaron B.; Miller, Larry R.; Shewchuk, Lisa M.; Wells-Knecht, Kevin J.; Willard, Derril H., Jr.; Wright, Lois L.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(19), 4897-4902
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:379687
GI

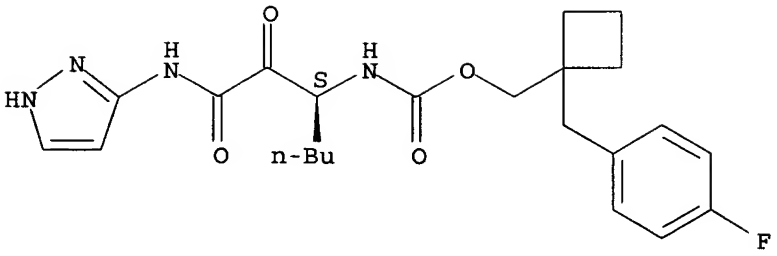


I

AB A series of keto amides were synthesized and evaluated for inhibitory activity against cathepsin K. Exploration of the interactions between achiral P2 substituents and the cysteine protease based on mol. modeling suggestions resulted in potent cathepsin K inhibitors that demonstrated high selectivity vs. cathepsins B, H, and L. Subsequent modifications of the P3, P1, and P1' moieties afforded orally bioavailable inhibitors, such as I.

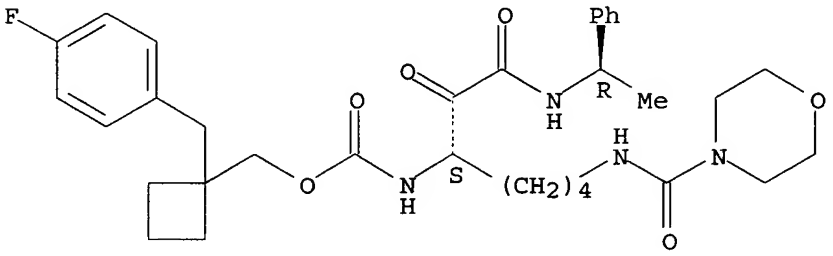
IT ***568590-73-8P***
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of potent and selective P2-P3 keto amide inhibitors of cathepsin K with good pharmacokinetic properties)
RN 568590-73-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, [1-[(4-fluorophenyl)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



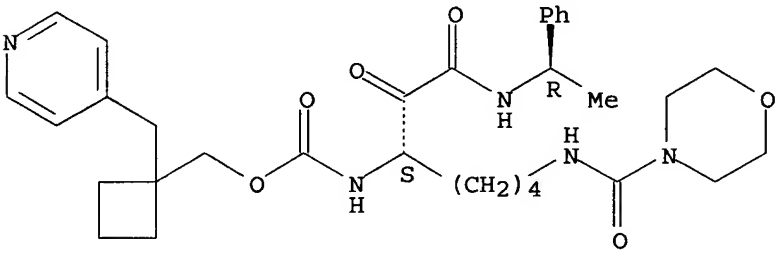
IT *568590-69-2P 568590-70-5P 568590-72-7P*
568590-75-0P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of potent and selective P2-P3 keto amide inhibitors of cathepsin K with good pharmacokinetic properties)
RN 568590-69-2 HCAPLUS
CN Carbamic acid, [(1S)-5-[(4-morpholinylcarbonyl)amino]-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(4-fluorophenyl)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 568590-70-5 HCAPLUS
CN Carbamic acid, [(1S)-5-[(4-morpholinylcarbonyl)amino]-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-(4-pyridinylmethyl)cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

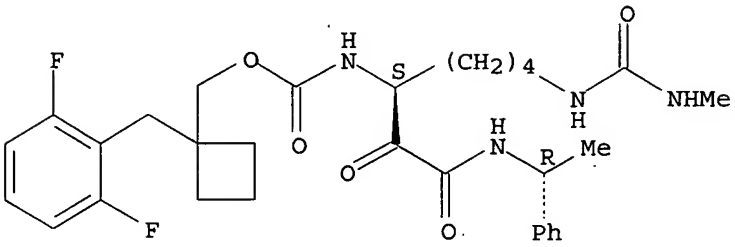
Absolute stereochemistry.



RN 568590-72-7 HCAPLUS
CN Carbamic acid, [(1S)-5-[[(methylamino)carbonyl]amino]-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(2,6-difluorophenyl)methyl]cyclobut

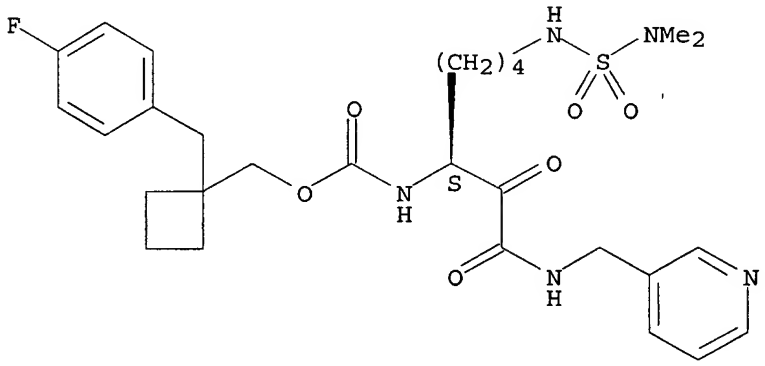
yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



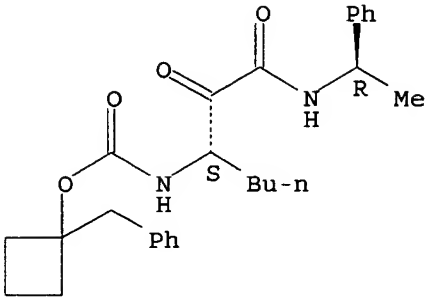
RN 568590-75-0 HCAPLUS
CN 3-Thia-2,4,10-triazaundecan-11-oic acid, 2-methyl-9-[oxo[(3-pyridinylmethyl)amino]acetyl]-, [1-[(4-fluorophenyl)methyl]cyclobutyl]methyl ester, 3,3-dioxide, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



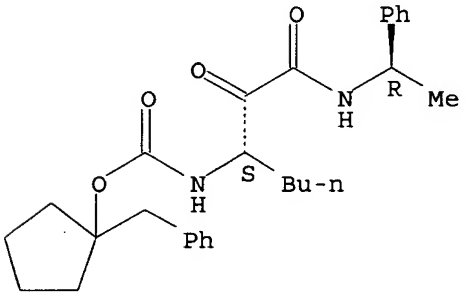
IT ***568590-60-3P 568590-61-4P 568590-63-6P 568590-64-7P 568590-65-8P 568590-66-9P 568590-67-0P 784181-99-3P 784182-00-9P 784182-01-0P***
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of potent and selective P2-P3 keto amide inhibitors of cathepsin K with good pharmacokinetic properties)
RN 568590-60-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, 1-(phenylmethyl)cyclobutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



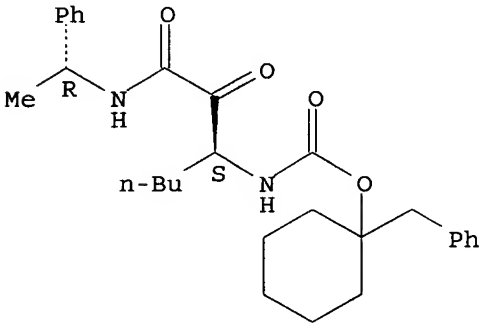
RN 568590-61-4 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, 1-(phenylmethyl)cyclopentyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



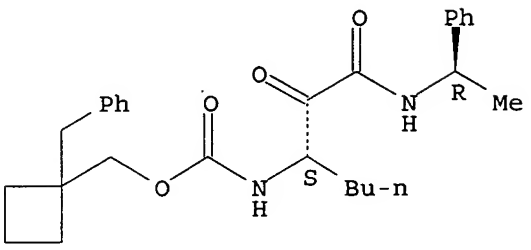
RN 568590-63-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, 1-(phenylmethyl)cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



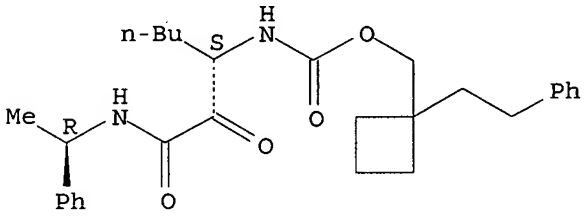
RN 568590-64-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-(phenylmethyl)cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



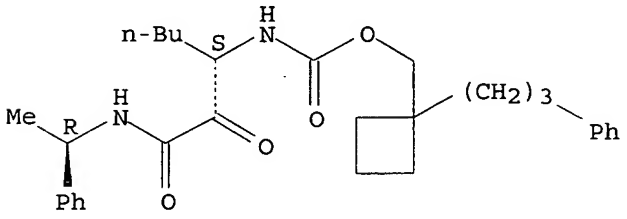
RN 568590-65-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-(2-phenylethyl)cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



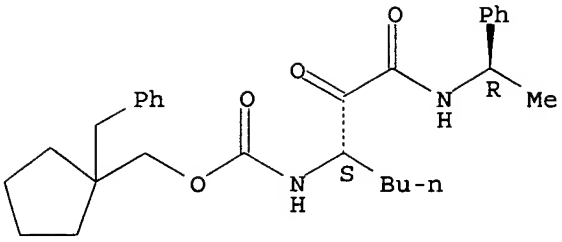
RN 568590-66-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-(3-phenylpropyl)cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



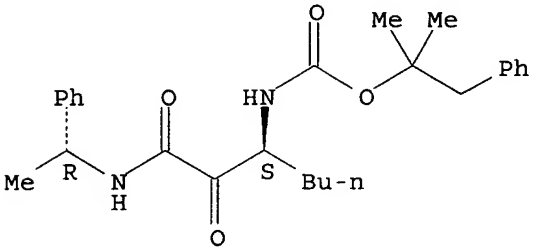
RN 568590-67-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-(phenylmethyl)cyclopentyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



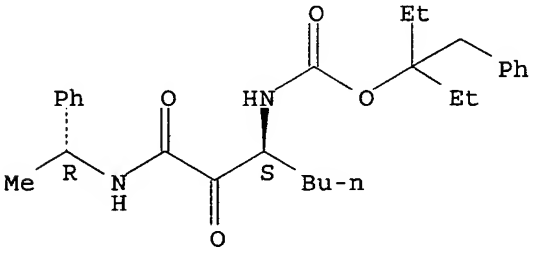
RN 784181-99-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, 1,1-dimethyl-2-phenylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



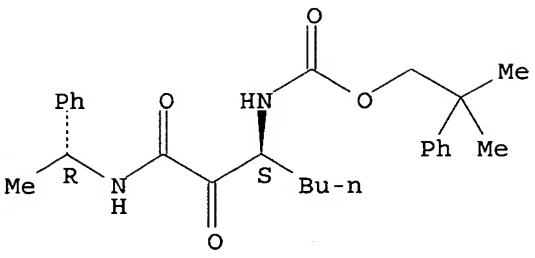
RN 784182-00-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, 1-ethyl-1-(phenylmethyl)propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 784182-01-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, 2-methyl-2-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Barrett, D	2004	14	2543	Bioorg Med Chem Lett	HCAPLUS
Boros, E	2004	14	3425	Bioorg Med Chem Lett	HCAPLUS
Catalano, J	2004	14	275	Bioorg Med Chem Lett	HCAPLUS
Catalano, J	2004	14	719	Bioorg Med Chem Lett	HCAPLUS
Deaton, D	2004	42	245	No publication given	HCAPLUS
Dressman, J	1998	15	11	Pharm Res	HCAPLUS
Einhorn, T	1996		3	Osteoporosis	
Finkel'Shtein, E	1980	20	75	Neftekhimiya	HCAPLUS
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Semple, J	2000	2	2769	Org Lett	HCAPLUS
Somoza, J	2002	322	559	J Mol Biol	HCAPLUS
Stroup, G	2001	16	1739	J Bone Miner Res	HCAPLUS
Tavares, F	2004	47	588	J Med Chem	HCAPLUS
Turk, D	1998	379	137	Biol Chem	HCAPLUS
Wasserman, H	1997	62	8972	J Org Chem	HCAPLUS
Weber, W	1972		1637	Tetrahedron Lett	HCAPLUS

L26 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:729346 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 141:388147
TITLE: Ketoamide-Based Inhibitors of Cysteine Protease, Cathepsin K: P3 Modifications
AUTHOR(S): Tavares, Francis X.; Deaton, David N.; Miller, Larry R.; Wright, Lois L.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(21), 5057-5068
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:388147
AB Osteoporosis is a disease characterized by skeletal fragility. Cathepsin K, a lysosomal cysteine protease, has been implicated in the osteoclast mediated bone resorption. Inhibitors of this protease could potentially treat this skeletal disease. The present work describes exploration of the spatial requirements of the S3 subsite by the use of various sterically demanding P3 substituents. Sulfur and oxygen linked heterocycles as well as those without heteroatom linkers were found to provide potent inhibitors of cathepsin K. Representative examples from

these series also afforded quite good selectivity ratios against most cathepsins tested. The tolerability of the S3 subsite for sterically demanding groups that provide potency and selectivity enhances the attractiveness of P3 changes to improve the physiochem. properties of inhibitors in the developments of compds. for the treatment of osteoporosis.

IT ***568590-78-3P 568590-79-4P 568590-80-7P 568590-81-8P 568590-82-9P 568590-83-0P 568590-84-1P 568590-85-2P 568590-86-3P 568590-87-4P 568590-88-5P 568590-89-6P 568590-90-9P 568590-91-0P 568590-92-1P 568590-93-2P 568590-94-3P 568590-95-4P 568590-96-5P 568590-97-6P 568590-98-7P 787604-46-0P***

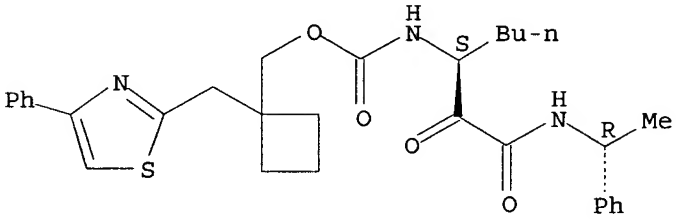
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(ketoamide-based inhibitors of cysteine protease, cathepsin K by P3 modifications)

RN 568590-78-3 HCAPLUS

CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(4-phenyl-2-thiazolyl)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

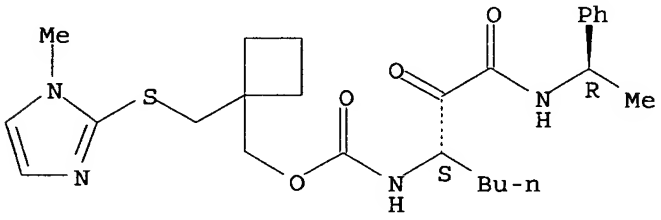
Absolute stereochemistry.



RN 568590-79-4 HCAPLUS

CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[(1-methyl-1H-imidazol-2-yl)thio]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

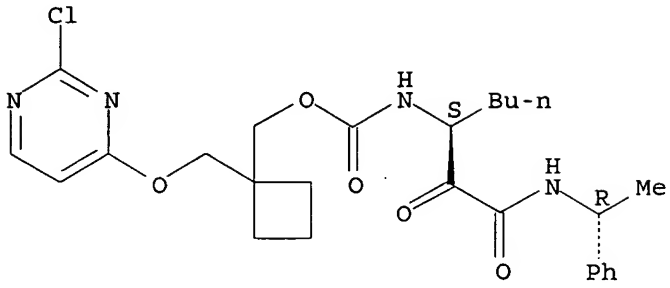
Absolute stereochemistry.



RN 568590-80-7 HCAPLUS

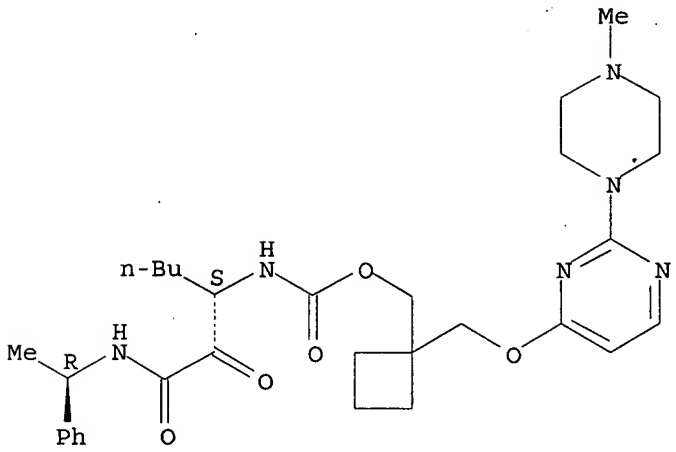
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[(2-chloro-4-pyrimidinyl)oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



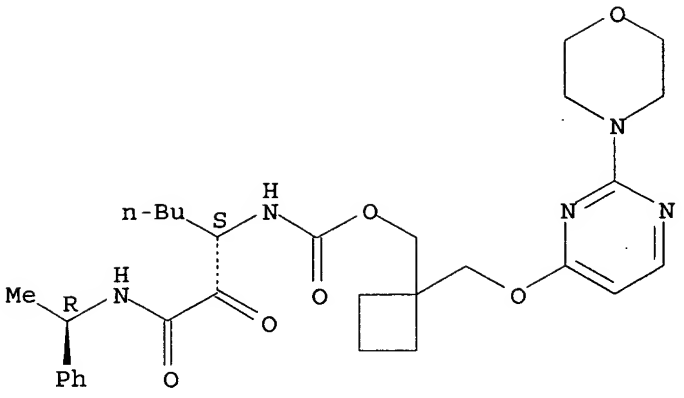
RN 568590-81-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[[2-(4-methyl-1-piperazinyl)-4-pyrimidinyl]oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



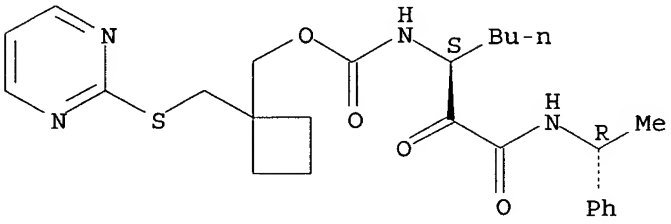
RN 568590-82-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[[2-(4-morpholinyl)-4-pyrimidinyl]oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



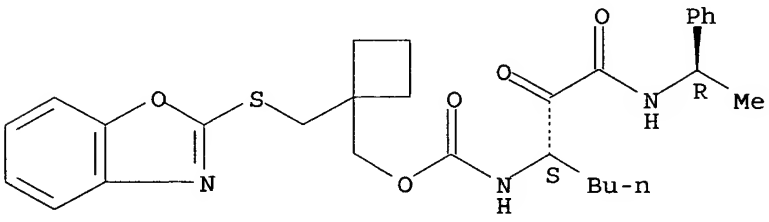
RN 568590-83-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(2-pyrimidinylthio)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



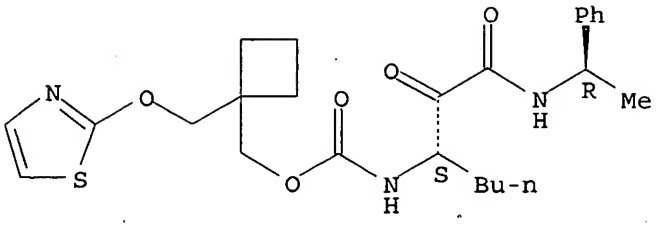
RN 568590-84-1 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(2-benzoxazolylthio)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



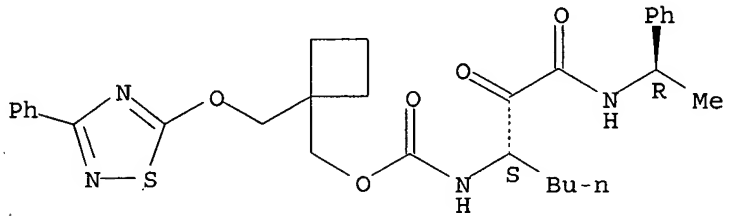
RN 568590-85-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(2-thiazolyloxy)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



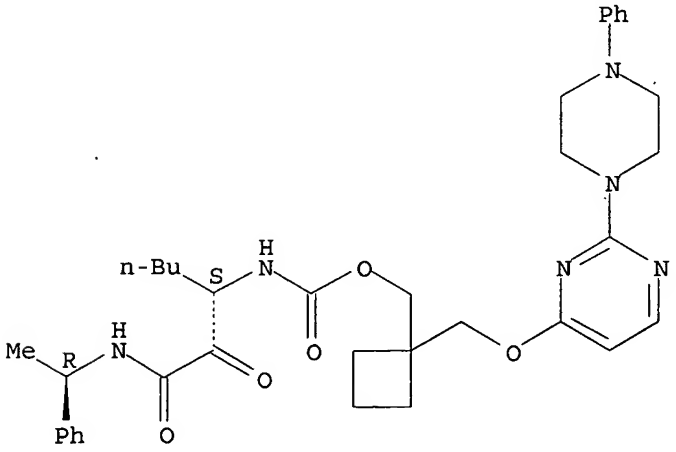
RN 568590-86-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[(3-phenyl-1,2,4-thiadiazol-5-yl)oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



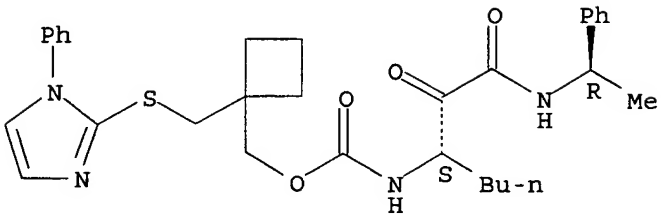
RN 568590-87-4 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[[2-(4-phenyl-1-piperazinyl)-4-pyrimidinyl]oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



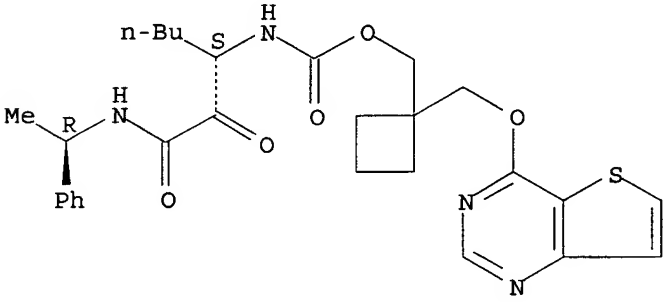
RN 568590-88-5 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[(1-phenyl-1H-imidazol-2-yl)thio]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



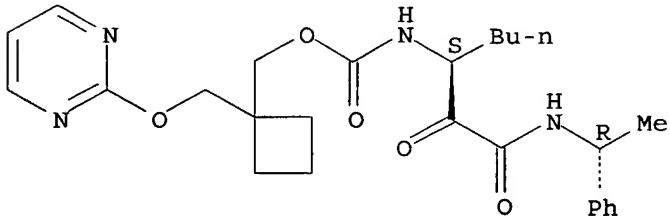
RN 568590-89-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(thieno[3,2-d]pyrimidin-4-yloxy)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



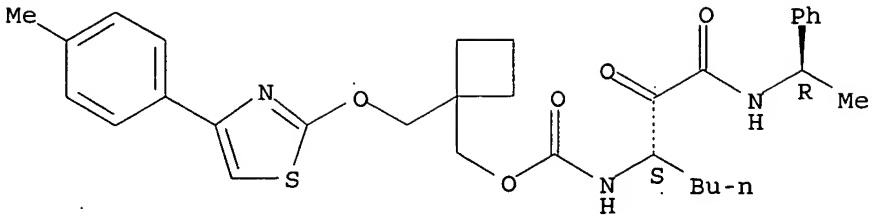
RN 568590-90-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(2-pyrimidinyloxy)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



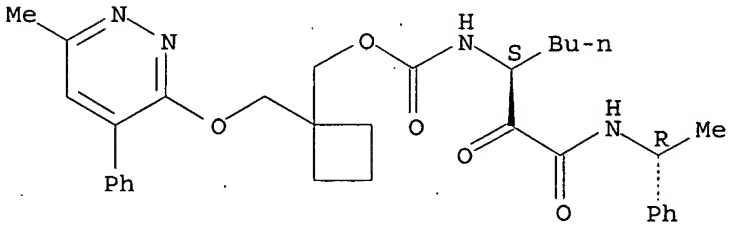
RN 568590-91-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[[4-(4-methylphenyl)-2-thiazolyl]oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



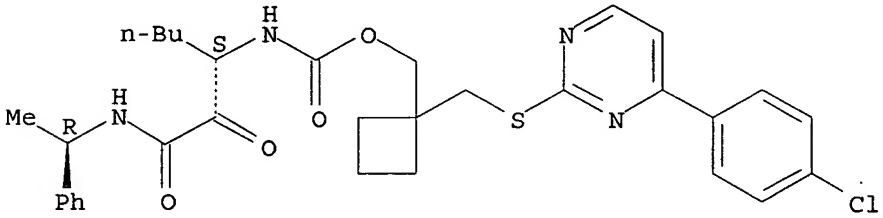
RN 568590-92-1 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[(6-methyl-4-phenyl-3-pyridazinyl)oxy]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



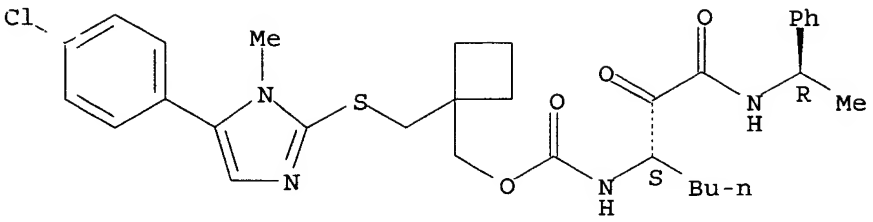
RN 568590-93-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[[4-(4-chlorophenyl)-2-pyrimidinyl]thio]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



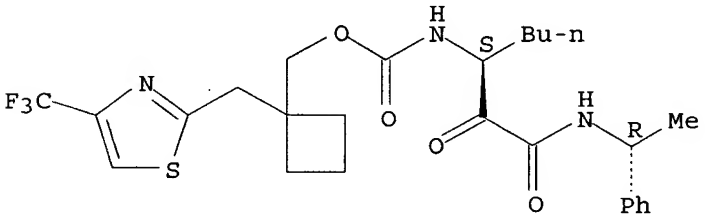
RN 568590-94-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[[5-(4-chlorophenyl)-1-methyl-1H-imidazol-2-yl]thio]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



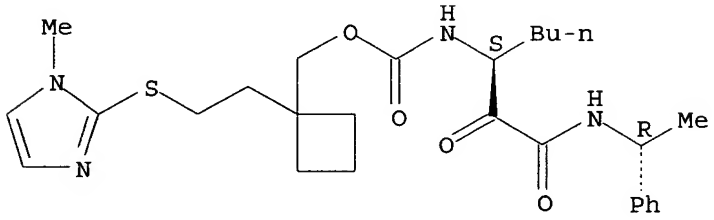
RN 568590-95-4 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[[4-(trifluoromethyl)-2-thiazolyl]methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



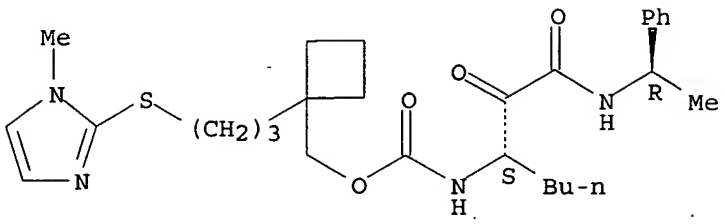
RN 568590-96-5 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[2-[(1-methyl-1H-imidazol-2-yl)thio]ethyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



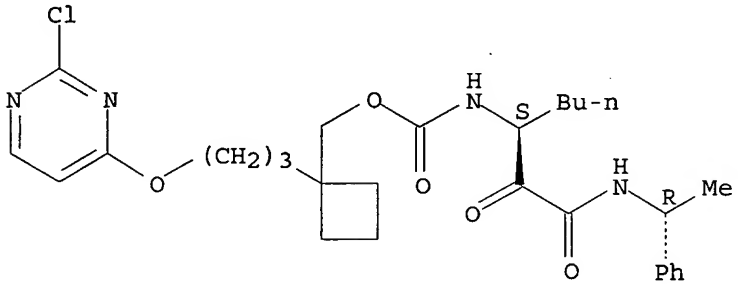
RN 568590-97-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[3-[(1-methyl-1H-imidazol-2-yl)thio]propyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



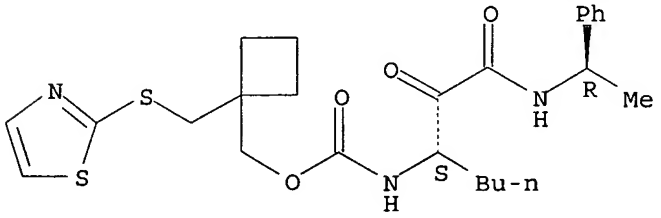
RN 568590-98-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[3-[(2-chloro-4-pyrimidinyl)oxy]propyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 787604-46-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, [1-[(2-thiazolylthio)methyl]cyclobutyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Altmann, E	2002	45	2352	J Med Chem	HCAPLUS
Ando, R	1999	7	571	Bioorg Med Chem	HCAPLUS
Ando, R	1993	115	1174	J Am Chem Soc	HCAPLUS
Baron, R	1990		3	Primer on the Metabo	
Barrett, D	2004	14	2543	Bioorg Med Chem Lett	HCAPLUS
Brisson, J	1986	261	9087	J Biol Chem	HCAPLUS
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Buhling, F	2000	477	241	Adv Exp Med Biol	HCAPLUS
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Desjarlais, R	1913	35	9114	J Am Chem Soc	
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Leung, D	2000	43	305	J Med Chem	HCAPLUS
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Palmer, J	1995	38	3193	J Med Chem	HCAPLUS
Robichaud, J	2003	46	3709	J Med Chem	HCAPLUS
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Semple, J	2000	2	2769	Org Lett	HCAPLUS
Shi, G	1995	357	129	FEBS Lett	HCAPLUS
Stroup, G	2001	16	1739	J Bone Miner Res	HCAPLUS
Szpaderska, A	2001	61	3493	Cancer Res	HCAPLUS
Tavares, F	2004	47	588	J Med Chem	HCAPLUS
Turk, B	2000	1477	98	Biochim Biophys Acta	HCAPLUS
Turk, V	2001	20	4629	EMBO J	HCAPLUS
Votta, B	1997	12	1396	J Bone Miner Res	HCAPLUS
Yamashita, D	2000	6	1	Curr Pharm Des	HCAPLUS
Yamashita, D	1997	119	11351	J Am Chem Soc	HCAPLUS
Yasuma, T	1998	41	4301	J Med Chem	HCAPLUS

L26 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:729345 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 141:374414
TITLE: Potent and Selective Ketoamide-Based Inhibitors of Cysteine Protease, Cathepsin K
AUTHOR(S): Tavares, Francis X.; Deaton, David N.; Miller, Aaron B.; Miller, Larry R.; Wright, Lois L.; Zhou, Hui-Qiang
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(21), 5049-5056

CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:374414

AB Cathepsin K, a lysosomal cysteine protease of the papain superfamily, is abundantly and selectively expressed in osteoclasts, suggesting that this enzyme is crucial for bone resorption. Prevention of osteoclast-mediated bone resorption via inhibition of cathepsin K could be an effective approach to prevent osteoporosis. Potent and selective reversible ketoamide-based inhibitors have been identified in the present study. Using a known crystal structure of a ketoamide-based inhibitor, information from residues that form the P2/P3 pocket was used in the design of inhibitors that could allow for gains in selectivity and potency. Further, incorporation of P' selective heterocycles, along with the P2/P3 modifications, is also described. These modifications have resulted in potent and selective cathepsin K inhibitors that allow for improvements in their physiochem. properties and represent a viable lead series for the discovery of new therapies for the prevention and treatment of osteoporosis.

IT ***783305-80-6P 783305-81-7P 783305-82-8P***
783305-83-9P 783305-84-0P 783305-93-1P
783305-94-2P 783305-95-3P 783305-96-4P
783305-99-7P 783306-00-3P 783306-01-4P
783306-02-5P 783306-03-6P 783306-04-7P
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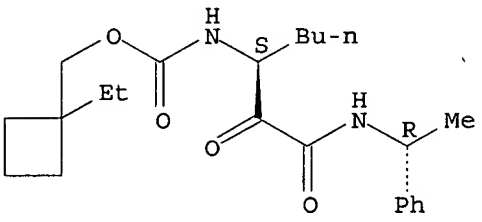
783306-08-1P 783306-09-2P 783306-10-5P
783306-11-6P 783306-12-7P 783306-13-8P
851591-68-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(potent and selective ketoamide-based inhibitors of cysteine protease, cathepsin K)

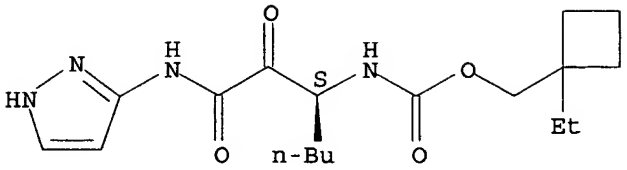
RN 783305-80-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



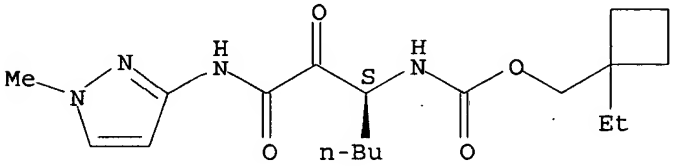
RN 783305-81-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



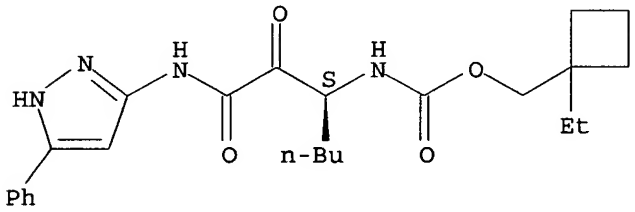
RN 783305-82-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-methyl-1H-pyrazol-3-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



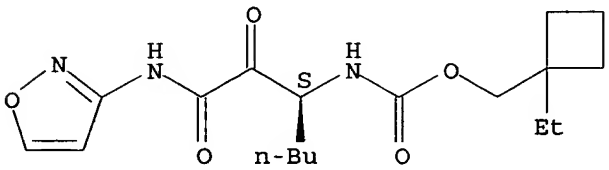
RN 783305-83-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[(5-phenyl-1H-pyrazol-3-yl)amino]acetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



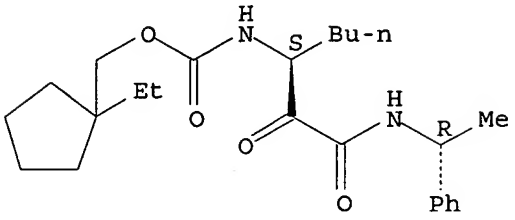
RN 783305-84-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[(3-isoxazolylamino)oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



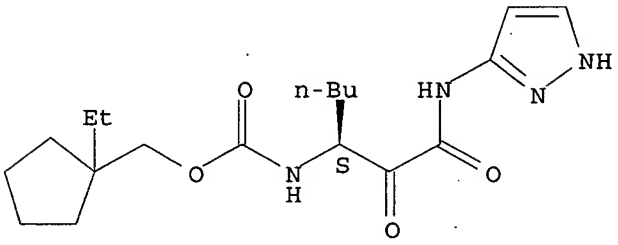
RN 783305-93-1 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1-ethylcyclopentyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



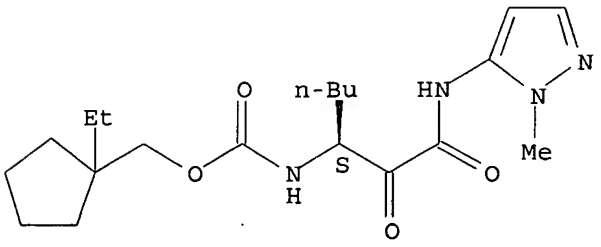
RN 783305-94-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1-ethylcyclopentyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



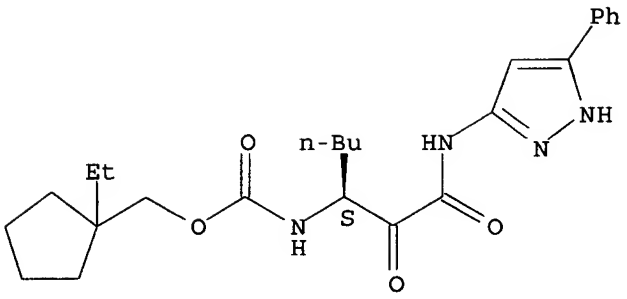
RN 783305-95-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-methyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclopentyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



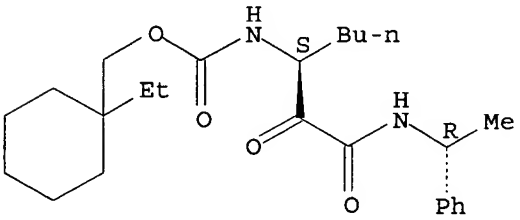
RN 783305-96-4 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[(5-phenyl-1H-pyrazol-3-yl)amino]acetyl]pentyl]-, (1-ethylcyclopentyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



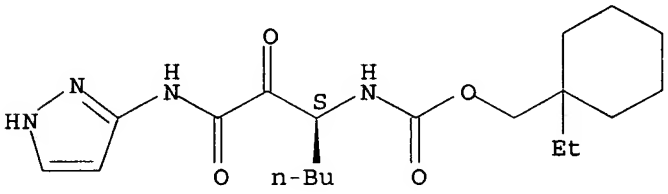
RN 783305-99-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, (1-ethylcyclohexyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



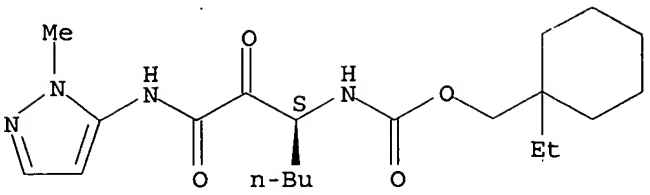
RN 783306-00-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1-ethylcyclohexyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



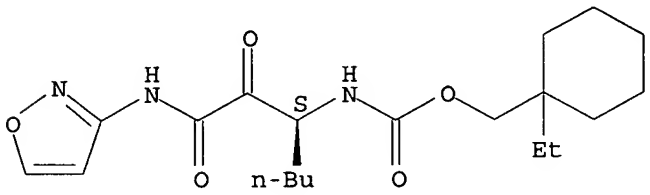
RN 783306-01-4 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-methyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclohexyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



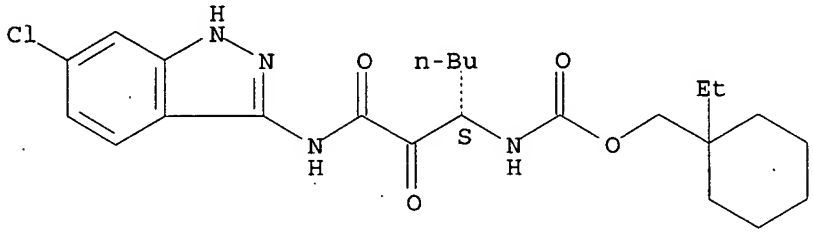
RN 783306-02-5 HCAPLUS
CN Carbamic acid, [(1S)-1-[(3-isoxazolylamino)oxoacetyl]pentyl]-, (1-ethylcyclohexyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



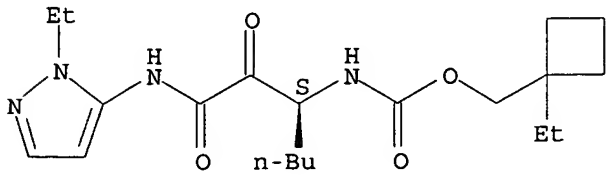
RN 783306-03-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(6-chloro-1H-indazol-3-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclohexyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 783306-04-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-ethyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

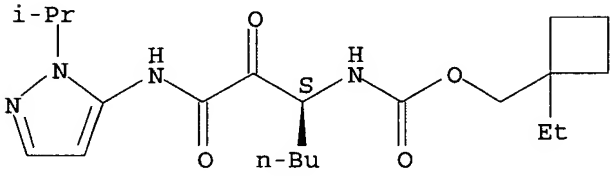
Absolute stereochemistry.



RN 783306-05-8 HCAPLUS

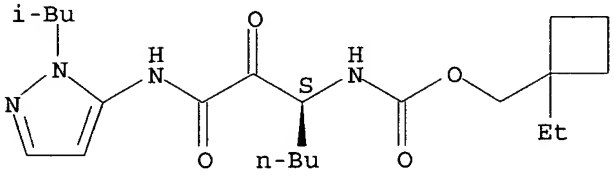
CN Carbamic acid, [(1S)-1-[[[1-(1-methylethyl)-1H-pyrazol-5-yl]amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



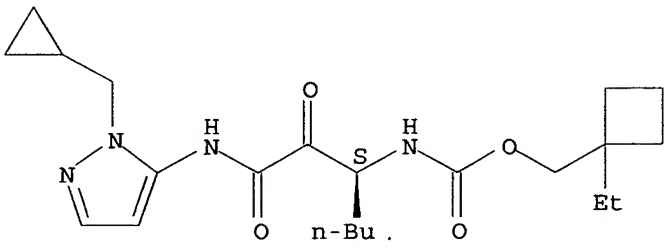
RN 783306-06-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[[[1-(2-methylpropyl)-1H-pyrazol-5-yl]amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



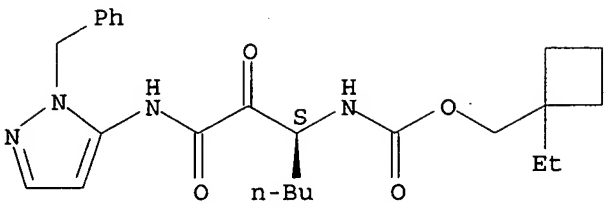
RN 783306-07-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[[[1-(cyclopropylmethyl)-1H-pyrazol-5-yl]amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



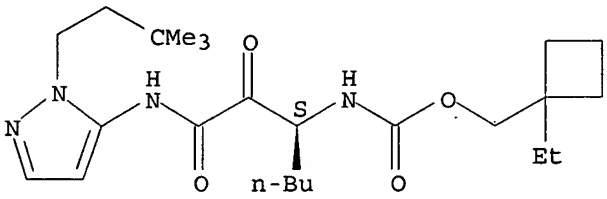
RN 783306-08-1 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[1-(phenylmethyl)-1H-pyrazol-5-yl]amino]acetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



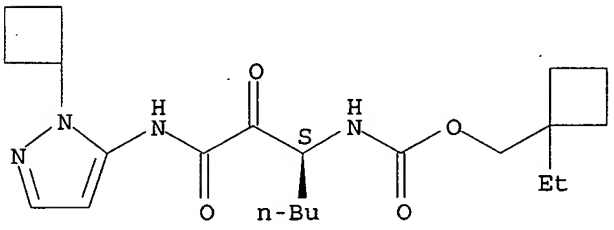
RN 783306-09-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[[[1-(3,3-dimethylbutyl)-1H-pyrazol-5-yl]amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 783306-10-5 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-cyclobutyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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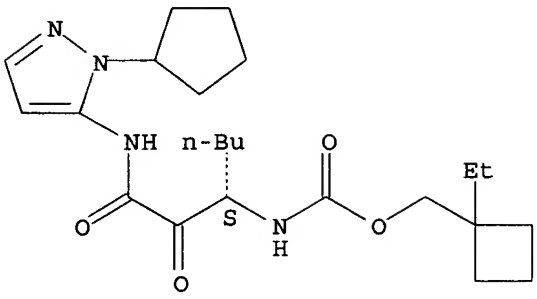
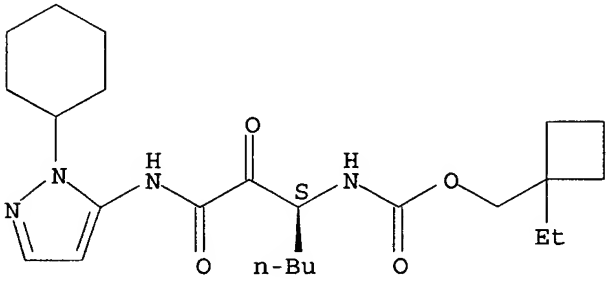
CN Carbamic acid, [(1S)-1-[[(1-cyclopentyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



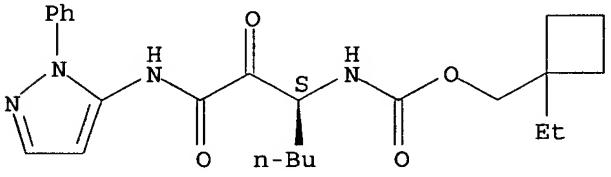
RN 783306-12-7 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-cyclohexyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



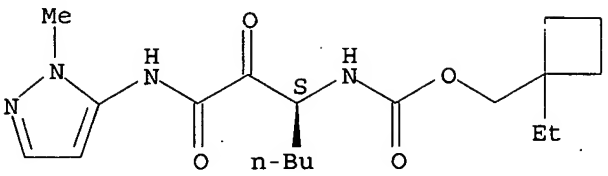
RN 783306-13-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[(1-phenyl-1H-pyrazol-5-yl)amino]acetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851591-68-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(1-methyl-1H-pyrazol-5-yl)amino]oxoacetyl]pentyl]-, (1-ethylcyclobutyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Altmann, E	2002	45	2352	J Med Chem	HCAPLUS
Ando, R	1999	7	571	Bioorg Med Chem	HCAPLUS
Ando, R	1993	115	1174	J Am Chem Soc	HCAPLUS
Baron, R	1990		3	Primer on the Metabo	
Brisson, J	1986	261	9087	J Biol Chem	HCAPLUS
Bromme, D	1996	315	85	Biochem J	HCAPLUS
Bromme, D	1995	376	379	Biol Chem Hoppe-Seyl	HCAPLUS
Buhling, F	2000	477	241	Adv Exp Med Biol	HCAPLUS
Cacciola, J	2000	10	1253	Bioorg Med Chem Lett	HCAPLUS
Catalano, J	2004	14	275	Bioorg Med Chem Lett	HCAPLUS
Catalano, J	2004	14	719	Bioorg Med Chem Lett	HCAPLUS
Dai, Y	2000	39	6498	Biochemistry	HCAPLUS
Delaisse, J	1987	8	305	Bone	HCAPLUS
Desjarlais, R	1998	120	9114	J Am Chem Soc	HCAPLUS
Dorgan, R	1980		938	J Chem Soc, Perkin T	HCAPLUS
Drake, F	1996	271	12511	J Biol Chem	HCAPLUS
Ege, G	1982	18	1267	J Heterocycl Chem	
Everts, V	1988	43	172	Calcif Tissue Int	HCAPLUS
Frigola, J	1989	24	435	Eur J Med Chem Chim	HCAPLUS
Gelb, B	1996	59	200	Biochem Mol Med	HCAPLUS
Gelb, B	1996	273	1236	Science	HCAPLUS
Gowen, M	1999	14	1654	J Bone Miner Res	HCAPLUS
Greenspan, P	2001	44	4524	J Med Chem	HCAPLUS
Harbeson, S	1994	37	2918	J Med Chem	HCAPLUS
Hashimoto, Y	2001	283	334	Biochem Biophys Res	HCAPLUS
Hu, L	1990	281	271	Arch Biochem Biophys	HCAPLUS
Inui, T	1997	272	8109	J Biol Chem	HCAPLUS
James, I	2001	276	11507	J Biol Chem	HCAPLUS
Johnson, M	1996	6	1050	Genome Res	HCAPLUS
Karanewsky, D	1998	8	2757	Bioorg Med Chem Lett	HCAPLUS
Kim, T	2004	14	87	Bioorg Med Chem Lett	HCAPLUS
Leung, D	2000	43	305	J Med Chem	HCAPLUS
Li, Z	2004	279	5470	J Biol Chem	HCAPLUS
Li, Z	1993	36	3472	J Med Chem	HCAPLUS
Liang, T	1987	252	626	Arch Biochem Biophys	HCAPLUS
Littlewood-Evans, A	1997	20	81	Bone	HCAPLUS
Majalli, A	1994	4	1965	Bioorg Med Chem Lett	
Marcus, R	1996			Osteoporosis, 1st ed	
Marquis, R	2001	44	1380	J Med Chem	HCAPLUS
Moon, J	1986	108	1350	J Am Chem Soc	HCAPLUS
Motyckova, G	2002	2	407	Curr Mol Med	HCAPLUS
Palmer, J	1995	38	3193	J Med Chem	HCAPLUS
Rosenthal, K	1997	38	1075	Tetrahedron Lett	HCAPLUS
Saftig, P	1998	95	13453	Proc Natl Acad Sci U	HCAPLUS
Schirmeister, T	1997	97	133	Chem Rev	
Setti, E	2003	13	2051	Bioorg Med Chem Lett	HCAPLUS

Shi, G	1995	357	129	FEBS Lett	HCAPLUS
Stroup, G	2001	16	1739	J Bone Miner Res	HCAPLUS
Szpaderska, A	2001	61	3493	Cancer Res	HCAPLUS
Tavares, F	2004	47	588	J Med Chem	HCAPLUS
Turk, B	2000	1477	98	Biochim Biophys Acta	HCAPLUS
Turk, V	2001	20	4629	EMBO J	HCAPLUS
Votta, B	1997	12	1396	J Bone Miner Res	HCAPLUS
Wasserman, H	1994	59	4364	J Org Chem	HCAPLUS
Yamashita, D	2000	6	1	Curr Pharm Des	HCAPLUS
Yamashita, D	1997	119	11351	J Am Chem Soc	HCAPLUS
Yasuma, T	1998	41	4301	J Med Chem	HCAPLUS

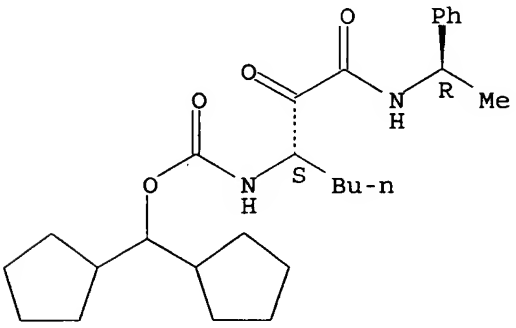
L26 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:51807 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 140:283250
TITLE: Design of small molecule ketoamide-based inhibitors of cathepsin K
AUTHOR(S): Catalano, John G.; Deaton, David N.; Long, Stacey T.; McFadyen, Robert B.; Miller, Larry R.; Payne, J. Alan; Wells-Knecht, Kevin J.; Wright, Lois L.
CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 719-722
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:283250

AB A novel series of ketoamide-based inhibitors of cathepsin K has been identified. Modifications to P2 and P3 elements were crucial to enhancing inhibitory activity. Although not optimized, a selected inhibitor was effective in attenuating type I collagen hydrolysis in a surrogate assay of bone resorption.

IT ***676235-41-9P***
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design of small mol. ketoamide-based inhibitors of cathepsin K)

RN 676235-41-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo[[(1R)-1-phenylethyl]amino]acetyl]pentyl]-, dicyclopentylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Adang, A	2002	45	4419	J Med Chem	HCAPLUS
Beevers, R	2002	12	641	Bioorg Med Chem Lett	HCAPLUS
Blume, H	1978	28	956	Arzneim Forsch	HCAPLUS
Catalano, J	2004	14	275	Bioorg Med Chem Lett	HCAPLUS
Conaway, H	1997	155	513	J Endocrinol	HCAPLUS
Dressman, J	1998	15	11	Pharm Res	HCAPLUS
Einhorn, T	1996		3	Osteoporosis	
Gollnick, K	1992	57	229	J Org Chem	HCAPLUS
Hahn, T	1984	114	1864	Endocrinol	HCAPLUS
Harbeson, S	1994	37	2918	J Med Chem	HCAPLUS
Irvine, J	1999	88	28	J Pharm Sci	HCAPLUS
Jones, D	1995	2	147	Lett Pept Sci	HCAPLUS
Kostewicz, E	2002	19	345	Pharm Res	HCAPLUS
Leung-Toung, R	2002	9	979	Curr Med Chem	HCAPLUS
Li, Z	2002	277	28669	J Biol Chem	HCAPLUS
Lubisch, W	2003	46	2404	J Med Chem	HCAPLUS
McQueney, M	1998	14	387	Protein Exp Purif	HCAPLUS
Prasad, J	1990	31	1803	Tetrahedron Lett	HCAPLUS
Semple, J	2000	2	2769	Org Lett	HCAPLUS
Somoza, J	2002	322	559	J Mol Biol	HCAPLUS
Stroup, G	2001	16	1739	J Bone Miner Res	HCAPLUS
Veber, D	2000		453	Proceedings of the A	HCAPLUS
Wasserman, H	1997	38	953	Tetrahedron Lett	HCAPLUS
Weber, W	1972	11	530	Angew Chem, Int Ed E	HCAPLUS
Yamashita, D	2000	6	1	Curr Pharm Des	HCAPLUS

L26 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:48265 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 140:236090
TITLE: α-Keto Amide Peptides: A Synthetic Strategy to Resin-Bound Peptide Isosteres for Protease Inhibitor Screening on Solid Support
AUTHOR(S): Papanikos, Alexandra; Meldal, Morten
CORPORATE SOURCE: Carlsberg Laboratory, Department of Chemistry, Center for Solid-Phase Organic Combinatorial Chemistry, Valby, DK-2500, Den.
SOURCE: Journal of Combinatorial Chemistry (2004), 6(2), 181-195
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:236090

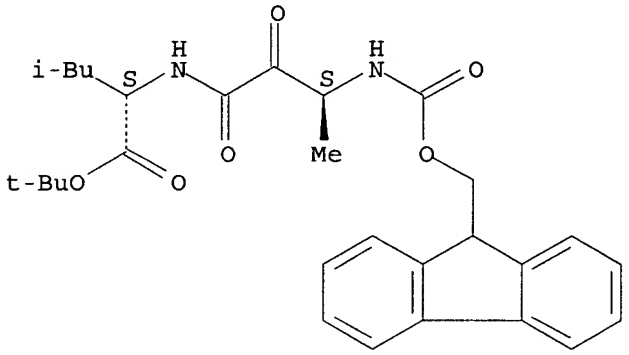
AB A synthetic strategy for the formation of resin-bound internal α-keto amide peptides suitable for protease inhibitor screening on solid support is presented. This general approach is based on the incorporation of α-keto amide building blocks during solid-phase peptide synthesis (SPPS). Such dipeptidyl building blocks were accessible using the acylcyanophosphorane methodol. The acid-labile α-keto carbonyl functionality was protected as a 1,3-dithiolane derivative This protective group is fully compatible with standard SPPS reaction conditions and can be efficiently removed with N-bromosuccinimide in 10% aqueous acetone. The α-keto amide peptides were assembled on SPOCC-1500 resin and were characterized with high-resolution magic angle spinning (HR-MAS) NMR on bead. The methodol. was evaluated and tested with a variety of building

blocks containing natural and nonnatural amino acid moieties.

IT ***667454-62-8P 667454-63-9P 667454-64-0P***
667454-65-1P 667454-66-2P 667454-67-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of resin-bound keto amide peptides using dithiolane protection for keto group)

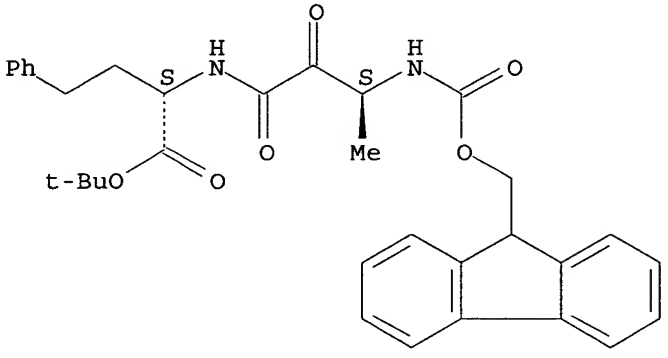
RN 667454-62-8 HCAPLUS
CN L-Leucine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



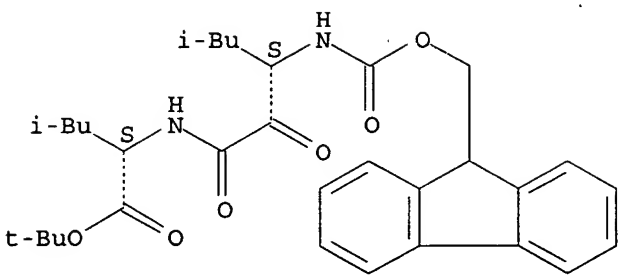
RN 667454-63-9 HCAPLUS
CN Benzenebutanoic acid, α-[[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxobutyl]amino]-, 1,1-dimethylethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



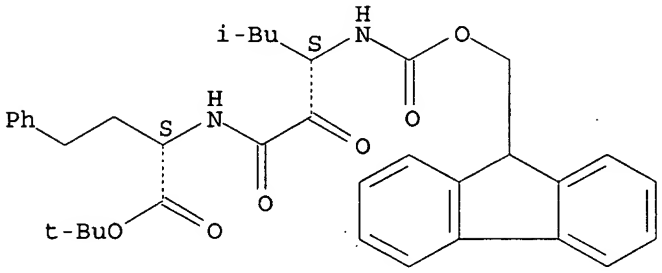
RN 667454-64-0 HCAPLUS
CN L-Leucine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-5-methyl-1,2-dioxohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



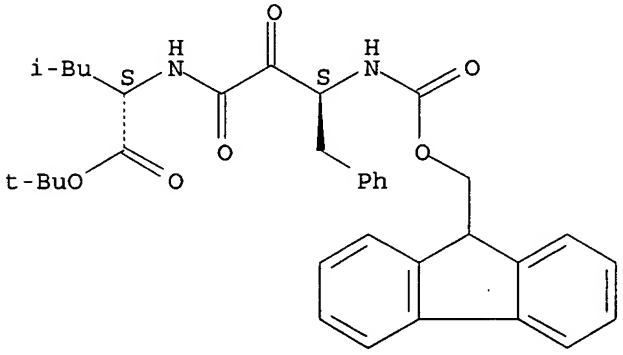
RN 667454-65-1 HCAPLUS
CN Benzenebutanoic acid, α-[[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-5-methyl-1,2-dioxohexyl]amino]-, 1,1-dimethylethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



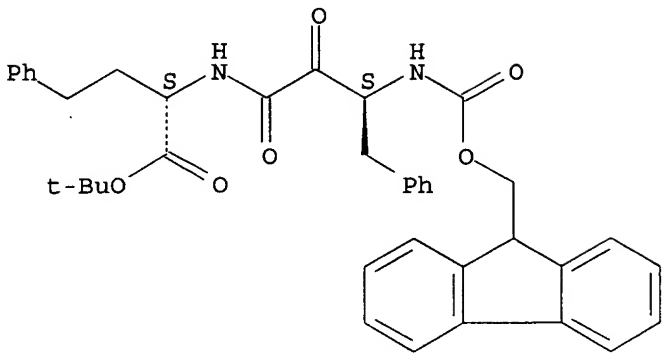
RN 667454-66-2 HCAPLUS
CN L-Leucine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxo-4-phenylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 667454-67-3 HCAPLUS
CN Benzenebutanoic acid, α-[[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxo-4-phenylbutyl]amino]-, 1,1-dimethylethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

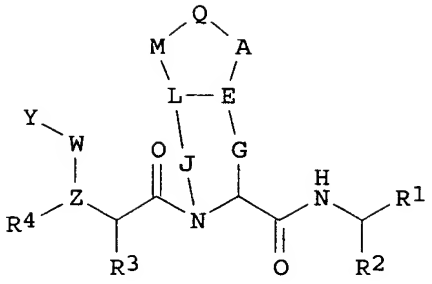
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Banfi, L	2002	43	4067	Tetrahedron Lett	HCAPLUS
Bates, G	1981	46	1745	J Org Chem	HCAPLUS
Bax, A	1986	108	2093	J Am Chem Soc	HCAPLUS
Bax, A	1985	63	207	J Magn Reson	HCAPLUS
Bertini, V	2000	65	4839	J Org Chem	HCAPLUS
Blankemeyer-Menge, B	1990	31	1701	Tetrahedron Lett	HCAPLUS
Boatman, P	1999	42	1367	J Med Chem	HCAPLUS
Brady, K	1999	7	621	Bioorg Med Chem	HCAPLUS
Buchardt, J	1999	5	2877	Chem Eur J	HCAPLUS
Cain, E	1975	16	1353	Tetrahedron Lett	
Carpino, L	1993	115	4397	J Am Chem Soc	HCAPLUS
Chapman, H	1997	59	63	Annu Rev Physiol	HCAPLUS
Charles, R	1999	42	1376	J Med Chem	
Chattopadhyaya, J	1973	14	3735	Tetrahedron Lett	
Corey, E	1971	36	3553	J Org Chem	HCAPLUS
Derome, A	1990	88	177	J Magn Reson	
Di Cera, E	1997	53	701	Cell Mol Life Sci	HCAPLUS
Ede, N	2000	6	11	J Pept Sci	HCAPLUS
Fusetani, N	1990	112	7053	J Am Chem Soc	HCAPLUS
Fusetani, N	1991	113	7811	J Am Chem Soc	HCAPLUS
Gelb, M	1985	24	1813	Biochemistry	HCAPLUS
Groth, T	2001	3	34	J Comb Chem	HCAPLUS
Halkes, K	2001	7	3584	Chem Eur J	HCAPLUS
Harbeson, S	1994	37	2918	J Med Chem	
Ho, T	1972		791	Chem Commun	HCAPLUS
Hu, L	1990	281	271	Arch Biochem Biophys	HCAPLUS
Hwang, T	1992	114	3157	J Am Chem Soc	HCAPLUS
Imperiali, B	1986	25	3760	Biochemistry	HCAPLUS
Kay, L	1992	114	10663	J Am Chem Soc	HCAPLUS
Knorr, R	1989	30	1927	Tetrahedron Lett	HCAPLUS
Kobayashi, J	1991	113	7812	J Am Chem Soc	HCAPLUS
Li, Z	1993	36	3472	J Med Chem	HCAPLUS
Lubisch, W	2002	12	373	Bioorg Med Chem Lett	
Lynas, J	1998	8	373	Bioorg Med Chem Lett	HCAPLUS
McKerrow, J	1996	6	1	Perspect Drug Discov	
Melnyk, O	2000	55	165	Biopolymers	HCAPLUS

Munzo, B	1994	2	1085	Bioorg Med Chem	
Olah, G	1982		965	Synthesis	HCAPLUS
Otto, H	1997	97	133	Chem Rev	HCAPLUS
Papanikos, A	2001	123	2176	J Am Chem Soc	HCAPLUS
Rademann, J	1999	121	5459	J Am Chem Soc	HCAPLUS
Ropp, G	1960	82	842	J Am Chem Soc	
Sheha, M	2000	35	887	Eur J Med Chem	HCAPLUS
Stang, P	1982		85	Synthesis	HCAPLUS
Tsuda, M	1996	49	890	J Antibiot	HCAPLUS
Venkatesan, N	2002	9	2243	Curr Med Chem	HCAPLUS
Villa, P	1997	22	388	Trends Biochem Sci	HCAPLUS
Wasserman, H	1994	59	4364	J Org Chem	HCAPLUS
Wasserman, H	1997	62	8972	J Org Chem	HCAPLUS
Wassermann, H	1993	58	4785	J Org Chem	
Weik, S	2003	42	2491	Angew Chem, Int Ed	HCAPLUS
Wu, Y	2000	41	2847	Tetrahedron Lett	HCAPLUS
Yang, Z	2002	4	1103	Org Lett	HCAPLUS

L26 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:912843 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 139:381756
TITLE: Preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus
INVENTOR(S): Saksena, Anil K.; Girijavallabhan, Viyyoor Moopil; Lovey, Raymond G.; Jao, Edwin; Bennett, Frank; Mccormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Chan, Tin-Yau; Liu, Yi-tsung; Zhu, Zhaoning; Njoroge, F. George; Arasappan, Ashok; Parekh, Tejal; Ganguly, Ashit K.; Chen, Kevin X.; Venkatraman, Srikanth; Vaccaro, Henry A.; Pinto, Patrick A.; Santhanam, Bama; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.; Wu, Wanli; Hendrata, Siska; Huang, Yuhua
PATENT ASSIGNEE(S): Schering Corporation, USA; Dendreon Corporation
SOURCE: U.S. Pat. Appl. Publ., 629 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003216325	A1	20031120	US 2001-908955		20010719
US 2004254117	A9	20041216			
US 7012066	B2	20060314			
CN 1498224	A	20040519	CN 2001-813111		20010719
ZA 2002010312	A	20040329	ZA 2002-10312		20021219
US 2006205672	A1	20060914	US 2005-241656		20050930
PRIORITY APPLN. INFO.:			US 2000-220108P	P	20000721
			US 2001-908955	A3	20010719

OTHER SOURCE(S): MARPAT 139:381756
GI



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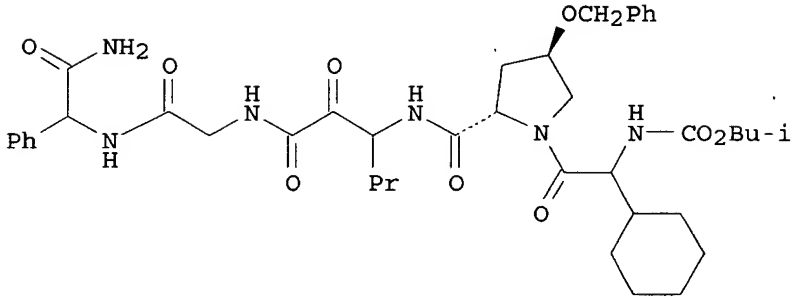


II

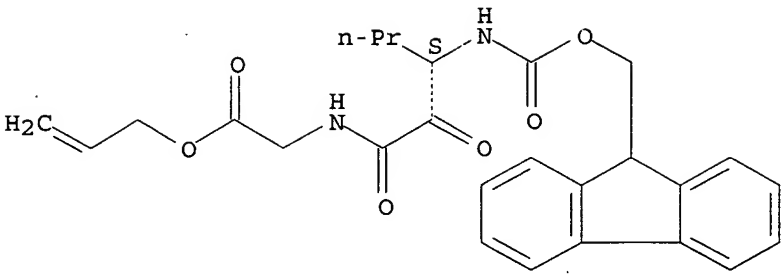
AB The invention discloses novel peptides I [Y is alkyl, alkylaryl, heteroalkyl, heteroaryl, aryl- or alkylheteroaryl, cycloalkyl, alkyloxy, alkylaryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkylarylamino, arylamino, heteroarylamino, cycloalkylamino, or heterocycloalkylamino; R1 is acyl; Z is O, N, CH or CR; R, R2-R4 are H, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, halo, (cycloalkyl)alkyl, or (heterocycloalkyl)alkyl; W, Q, G, J, L, M independently may be present or absent; W is CO, CS, C(:N-CN), or SO2; Q is CH, N, P, alkylidene, O, NR, S, or SO2; A is O, CH, alkylidene, NR, S, SO2, or a bond; E is CH, N, alkylidene, or a double bond; G is alkylidene; J is alkylidene, SO2, NH, NR, or O; L is CH, CR, O, S, or NR; M is O, NR, S, SO2, or alkylidene (with provisos)] which have HCV protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such compds. as well as methods of using them to treat disorders associated with the HCV protease. Thus, peptide II was prepared by the solid-phase method and showed Ki = 1-100 nM (category A) in the HCV continuous assay.

IT ***276888-38-1P***
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 276888-38-1 HCAPLUS

CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Agrawal	1999	30		Hepatology Supplemen	
Anon					
Anon					
Anon					
Anon					
Anon					
Anon					
Anon	1986			EP 0195212 A	HCAPLUS
Anon	1989			WO 8904669	HCAPLUS
Anon	1990			EP 0363284 A	HCAPLUS
Anon	1990			EP 381216	HCAPLUS
Anon	1991			EP 0423358 A1	HCAPLUS
Anon	1992			JP 04149166 A	HCAPLUS
Anon	1992			JP 4001140 A	
Anon	1992			WO 9211850	HCAPLUS
Anon	1994			WO 9400095	HCAPLUS
Anon	1995			EP 0672648 A1	HCAPLUS
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Anon	1996			WO 9640743 A	HCAPLUS
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Anon	1997			WO 9731937 A	HCAPLUS
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Anon	2001			WO 0140262	HCAPLUS

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Anon	1998	9	4	Bio World Today	
Asano	1994	47	557	Journal of Antibioti	HCAPLUS
Barlos	1991		513	Int. J. Pept. Protei	HCAPLUS
Bartenschlager	1995	69	198	Journal of Virology	HCAPLUS
Berenguer	1998	110	98	Proc. Assoc. Am. Phy	HCAPLUS
Bianchi	1996	237	239	Analytical Bichemist	HCAPLUS
Bouffard	1995	209	52	Virology	HCAPLUS
Casey	1998			US 5854001 A	HCAPLUS
Cho	1997	65	201	Journal of Virologic	HCAPLUS
Dasmahapatra	1998			US 5843752 A	HCAPLUS
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Elzouki	1997	27	42	J. Hepat.	HCAPLUS
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Hahm	1996	226	318	Virology	HCAPLUS
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Hanson	1996			US 5488067 A	HCAPLUS
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Heck	1989	27	345	Org. Reactions	
Holmberg	1979	B33	410	Acta Chem. Scand.	HCAPLUS
Hoofnagle	1997	336	347	New England Journal	MEDLINE
Houghton	1998			US 5712145 A	HCAPLUS
Hughes	1992	42	335	Org. Reactions	HCAPLUS
Ingallinella	1998	37	8906	Biochem	HCAPLUS
Ito	1996	77	1043	J. Gen. Virol	HCAPLUS
Kolb	1996			US 5496927 A	HCAPLUS
Kolb	1998			US 5849866 A	HCAPLUS
Kollykhalov	1994	68	7525	J. Virol.	
Komoda	1994	68	7351	J. Virol.	HCAPLUS
Landro	1997	36	9340	Biochem	HCAPLUS
Llinas-Brunet	1998	8	1713	Bioorg. Med. Chem. L	HCAPLUS
Lu	1996	93	1412	Proc. Natl. Acad. Sc	HCAPLUS
Marchetti	1999	S1	1000	Synlett	
Martin	1998	37	11459	Biochem	HCAPLUS
Martin	1997	10	607	Protein Eng.	HCAPLUS
Mizutani	1995	212	906	Biochemical and Biop	HCAPLUS
Mizutani	1996	227	822	Biochemical and Biop	HCAPLUS
Mizutani	1996		721	Journal of Virology	
Narjes	2000	39	1849	Biochemistry	HCAPLUS
Ogilvie	1997	40	4113	J. Med. Chem.	HCAPLUS
Patel, D	1993	36	2431	Journal of Medicinal	HCAPLUS
Pizzi	1994	91	888	Proc. Natl. Acad. Sc	HCAPLUS
Powers	1996			US 5514694 A	HCAPLUS
Powers	1998			US 5763576 A	HCAPLUS
Sali	1998		3392	Biochemistry	HCAPLUS
Scarselli	1997		4985	Journal of Virology	HCAPLUS
Schechter	1967	27		Biochemical and Biop	HCAPLUS
Shimizu	1994		8406	Journal of Virology	HCAPLUS
Steinkuhler	1998	37	8899	Biochemistry	MEDLINE
Sudo	1996	32	9	Antiviral Research	HCAPLUS
Takeshita	1997	274	242	Analytical Biochemis	
Takeuchi	1992			US 5162500 A	HCAPLUS
Takeuchi	1994			US 5359138 A	HCAPLUS
Taliani	1996	240	60	Analytical Biochemis	HCAPLUS

Taremi	1998	7	2143	Protein Science	HCAPLUS
Tong	1998	5	819	Nature Structural Bi	HCAPLUS
Tsuda	1996	49	287	The Journal of Antib	HCAPLUS
Tsuda	1996	49	890	The Journal of Antib	HCAPLUS
Tung	2001			US 6265380 B1	HCAPLUS
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Wang	1997			4th International Me	
Wasserman	1994	59	4364	J. Org. Chem.	HCAPLUS
Zhang		270	268	Analytical Biochemis	HCAPLUS
Zhang	1997		6208	Journal of Virology	HCAPLUS

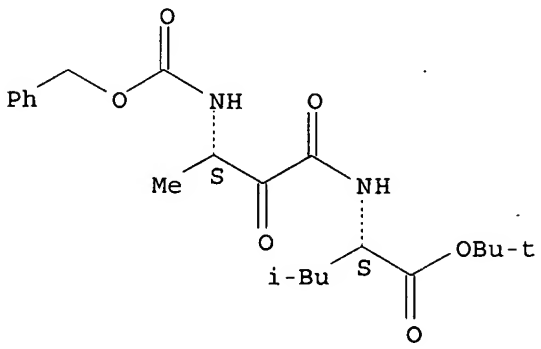
L26 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:645263 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 139:323774
TITLE: Application of acyl cyanophosphorane methodology to the synthesis of protease inhibitors: poststatin, eurystatin, phebestin, probestin and bestatin
AUTHOR(S): Wasserman, Harry H.; Petersen, Anders K.; Xia, Mingde
CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA
SOURCE: Tetrahedron (2003), 59(35), 6771-6784
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:323774

AB Full details are given for the syntheses of the protease inhibitors, poststatin and eurystatin by the acyl cyanophosphorane coupling procedure used for the formation of α-keto amides. We have also extended this methodol. to the syntheses of the related α-hydroxy amide natural products, phebestin, probestin and bestatin. The key step in the latter synthetic sequences involved diastereomeric selectivity in the reduction of the α-keto precursor to the corresponding α-hydroxy amide by the use of zinc borohydride.

IT ***199467-17-9P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-keto or α-hydroxy amides via acyl cyanophosphorane carbonyl insertion reaction)

RN 199467-17-9 HCAPLUS
CN L-Leucine, N-[(3S)-1,2-dioxo-3-[[(phenylmethoxy)carbonyl]amino]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RETABLE

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Aoyagi, T	1991	44	949	J Antibiot	HCAPLUS
Burkhart, J	1988	29	3433	Tetrahedron Lett	HCAPLUS
Burkhart, J	1990	31	1385	Tetrahedron Lett	HCAPLUS
Casapullo, A	1994	57	1227	J Nat Prod	HCAPLUS
Cutrona, K	1996	37	5045	Tetrahedron Lett	HCAPLUS
Edwards, P	1992	114	1854	J Am Chem Soc	HCAPLUS
Fusetani, N	1993	93	1793	Chem Rev	HCAPLUS
Fusetani, N	1990	112	7053	J Am Chem Soc	HCAPLUS
Fusetani, N	1991	113	7811	J Am Chem Soc	HCAPLUS
Gunasekera, S	1994	57	79	J Nat Prod	HCAPLUS
Hagihara, M	1992	114	6570	J Am Chem Soc	HCAPLUS
Iwanowicz, E	1992	2	1607	Biomed Chem Lett	HCAPLUS
Kobayashi, J	1991	113	7812	J Am Chem Soc	HCAPLUS
Mierzwa, R	1994	57	175	J Nat Prod	HCAPLUS
Nagai, M	1991	44	956	J Antibiot	HCAPLUS
Orita, M	1995	48	1430	J Antibiot	HCAPLUS
Peet, N	1990	33	394	J Med Chem	HCAPLUS
Rappe, C	1973	53	123	Organic Syntheses	HCAPLUS
Still, W	1978	43	2923	J Org Chem	HCAPLUS
Suzuki, K	1994	47	982	J Antibiot	HCAPLUS
Swersey, J	1994	57	842	J Nat Prod	HCAPLUS
Takeuchi, T	1994			US 5359138	HCAPLUS
Toda, S	1992	45	1573	J Antibiot	HCAPLUS
Toda, S	1992	45	1580	J Antibiot	HCAPLUS
Toda, S	1992	45	1580	J Antibiot	HCAPLUS
Tsuda, M	1996	49	281	J Antibiot	HCAPLUS
Tsuda, M	1996	49	287	J Antibiot	HCAPLUS
Tsuda, M	1991		223	Pept Chem	HCAPLUS
Wasserman, H	1993	58	4785	J Org Chem	HCAPLUS
Wasserman, H	1994	59	4364	J Org Chem	HCAPLUS
Wasserman, H	1997	62	8972	J Org Chem	HCAPLUS
Wasserman, H	2002	58	6277	Tetrahedron	HCAPLUS
Wasserman, H	1997	38	953	Tetrahedron Lett	HCAPLUS
Wasserman, H	1999	40	6163	Tetrahedron Lett	HCAPLUS

L26 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:591204 HCAPLUS <<LOGINID::20061206>>

DOCUMENT NUMBER: 139:149928

TITLE: Preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus

INVENTOR(S): Saksena, Anil K.; Girijavallabhn, Viyyoor M.; Lovey, Raymond G.; Jao, Edwin; Bennett, Frank; McCormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Chan, Tin-yau; Liu, Yi-tsung; Zhu, Zhaoning; Njoroge, George F.; Arasappan, Ashok; Parekh, Tejal; Ganguly, Ashit K.; Chen, Kevin X.; Venkatraman, Srikanth; Vaccaro, Henry A.; Pinto, Patrick A.; Santhanam, Bama; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.; Wu, Wanli; Hendrata, Siska; Huang, Yuhua; Wong, Jesse K.; Nair, Latha G.

PATENT ASSIGNEE(S): Schering Corporation, USA; Corvas International, Inc.; Dendreon Corp.

SOURCE: PCT Int. Appl., 633 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062265	A2	20030731	WO 2003-US1430	20030116
WO 2003062265	A3	20040916		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473032	AA	20030731	CA 2003-2473032	20030116
EP 1481000	A2	20041201	EP 2003-731956	20030116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003006931	A	20050419	BR 2003-6931	20030116
CN 1633446	A	20050629	CN 2003-805933	20030116
JP 2005524628	T2	20050818	JP 2003-562142	20030116
NO 2004002792	A	20041015	NO 2004-2792	20040702
PRIORITY APPLN. INFO.:			US 2002-52386 A	~~20020118~~
			WO 2003-US1430 W	20030116

OTHER SOURCE(S): MARPAT 139:149928
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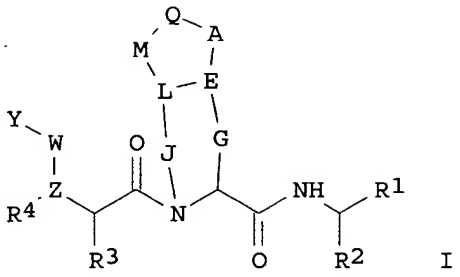

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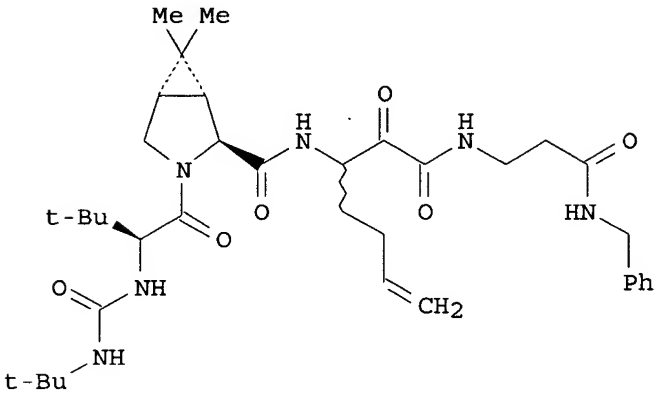


II

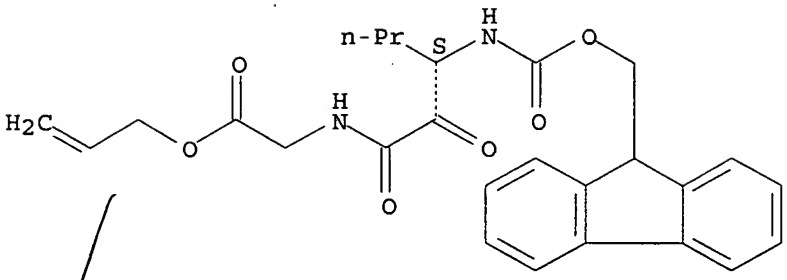
AB The invention discloses novel peptides I [Y is alkyl, alkylaryl, heteroalkyl, heteroaryl, aryl- or alkylheteroaryl, cycloalkyl, alkyloxy, alkylaryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkylarylamino, arylamino, heteroarylamino, cycloalkylamino, or heterocycloalkylamino; R1 is acyl; Z is selected from O, N, CH or CR; R, R2-R4 are H, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, halo, (cycloalkyl)alkyl, or (heterocycloalkyl)alkyl; W, Q, G, J, L, M independently may be present or absent; W is CO, CS, C(:N-CN), or SO2; Q is CH, N, P, alkylidene, O, NR, S, or SO2; A is O, CH, alkylidene, NR, S, SO2, or a bond; E is CH, N, alkylidene, or a double bond; G is alkylidene; J is alkylidene, SO2, NH, NR, or O; L is CH, CR, O, S, or NR; M is O, NR, S, SO2, or alkylidene (with provisos)] which have HCV protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such compds. as well as methods of using them to treat disorders associated with the HCV protease. Thus, peptide II was prepared and showed Ki = 1-100 nM (category A) in the HCV continuous assay.

IT ***276888-38-1P***
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 276888-38-1 HCAPLUS

CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



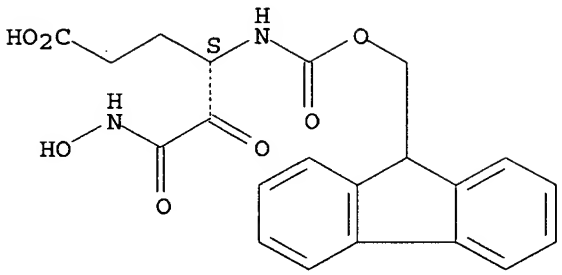
L26 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:521636 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 140:157168
TITLE: Potentiating vanadium-evoked glucose metabolism by novel hydroxamate derivatives
AUTHOR(S): Hindi, Sagit; Grossman, Dov P.; Goldwaser, Itzhak; Shechter, Yoram; Fridkin, Mati
CORPORATE SOURCE: Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel
SOURCE: Letters in Peptide Science (2003), Volume Date 2002, 9(6), 235-254
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB L-Glutamic acid (γ) monohydroxamate (L-Glu(γ)HXM) enhances the insulinomimetic activity of vanadium ions both in vitro and in vivo. Based on this ligand as a lead compound, and in order to delineate mol. features relevant to its anti-diabetic potential, 14 related derivs., including short peptides, were synthesized by solution as well as by solid phase methodologies. In addition, hydroxamate derivs. of (+) pantothenic acid and D-biotin were prepared The vanadium binding capacity of the hydroxamates synthesized was apparent, yet each had a different ligand-ions stoichiometry. The in vitro lipogenic potency of several compds. toward rat adipocytes was demonstrated. Thus, vanadium complexes of L-Gln(α)HXM, L-Glu(γ)HXM-Gly, L-Aad(δ)HXM, di-Glu-γ,γ-HXM and of (+) pantothenic acid hydroxamate exhibited 82, 79, 76, 39 and 39% of maximal insulin activity, resp. L-Aad(δ)HXM, L-Glu(γ)HXM-Gly and (+) pantothenic acid hydroxamate - by themselves - were found to possess 24, 14 and 10% of maximal insulin activity, resp. In vivo potency, however, of L-Gln(α)HXM vanadium complex in streptozocin-treated rat diabetic model was less apparent.

IT ***656831-32-2P***
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel hydroxamate derivs. preparation and potentiation of vanadium-evoked glucose metabolism)

RN 656831-32-2 HCAPLUS
CN Hexanoic acid, 4-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-6-(hydroxyamino)-5,6-dioxo-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Brichard, S	1990	39	1326	Diabetes	HCAPLUS
Brichard, S	1988	123	2048	Endocrinology	HCAPLUS
Brichard, S	1989	125	2510	Endocrinology	HCAPLUS
Brichard, S	1995	16	265	Trends Pharmacol Sci	HCAPLUS
Butler, A	1990			Vanadium in biologic	
Cohen, N	1995	95	2501	J Clin Invest	HCAPLUS
Cusi, K	2001	86	1410	J Clin Endocrinol Me	HCAPLUS
Elberg, G	1997	46	1684	Diabetes	HCAPLUS
Elberg, G	1994	269	9521	J Biol Chem	HCAPLUS
Fantus, I	1989	28	8864	Biochemistry	HCAPLUS
Floyd, C	1996	37	8045	Tetrahedron Lett	HCAPLUS
Goldfine, A	1995	80	3311	J Clin Endocrinol Me	HCAPLUS
Goldwaser, I	1999	274	26617	J Biol Chem	HCAPLUS
Goldwaser, I	2000	58	738	Mol Pharmacol	HCAPLUS
Halberstam, M	1996	45	659	Diabetes	HCAPLUS
Heyliger, C	1985	227	1474	Science	HCAPLUS
McNeill, J	1995	153	175	Mol Cell Biochem	HCAPLUS
Meyerovitch, J	1987	262	6658	J Biol Chem	HCAPLUS
Meyerovitch, J	1991	87	1286	J Clin Invest	HCAPLUS
Moody, A	1974	6	12	J, Horm Metab Res	HCAPLUS
Rodbell, M	1964	239	375	J Biol Chem	HCAPLUS
Sakurai, H	1995	214	1095	Biochem Biophys Res	HCAPLUS
Shechter, Y	1992	31	2063	Biochemistry	HCAPLUS
Shechter, Y	1990	39	1	Diabetes	HCAPLUS
Shechter, Y	1995	153	39	Mol Cell Biochem	HCAPLUS
Shechter, Y	1980	284	556	Nature	HCAPLUS
Shisheva, A	1991	129	2279	Endocrinology	HCAPLUS
Shisheva, A	1993	268	6463	J Biol Chem	HCAPLUS

L26 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133034 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 138:187774
TITLE: Preparation of α-ketoamide derivatives as cathepsin K inhibitors useful against bone disorders such as osteoporosis
INVENTOR(S): Barrett, David Gene; Deaton, David Norman; McFadyen, Robert Blount; Miller, Aaron Bayne; Ray, John Albert; Tavares, Francis Xavier; Zhou, Huiqiang
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Samano, Vicente
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013518	A1	20030220	WO 2002-US23255	20020723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1411933	A1	20040428	EP 2002-752509	20020723
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JP 2005504040	T2	20050210	JP 2003-518527	20020723
US 2005107616	A1	20050519	US 2003-485656	20020723
PRIORITY APPLN. INFO.:			US 2001-310169P	P 20010803
			WO 2002-US23255	W 20020723

OTHER SOURCE(S): MARPAT 138:187774

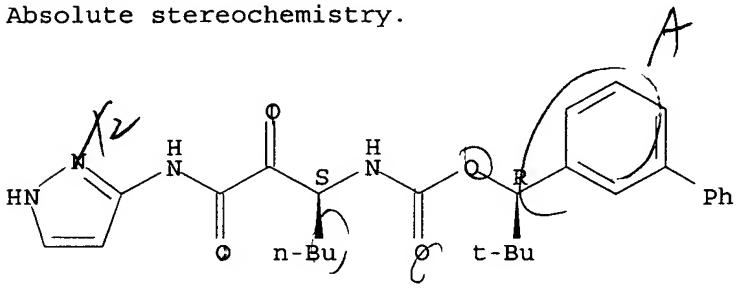
AB Bi-aryl/heteroaryl ketoamide derivs. ACH(R1)DC(O)NHCH(CH2CH2CH2CH2R2)C(O)C(O)NHZ (I; variables defined below; e.g. (1S)-2,2-dimethyl-1-[[3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]methyl]propyl (1S)-1-[oxo[(1H-pyrazol-5-ylmethyl)amino]acetyl]pentylcarbamate), useful as cathepsin K inhibitors, are described herein. The described invention also includes methods of making such I as well as methods of using the same in the treatment of disorders, including osteoporosis, associated with enhanced bone turnover which can ultimately lead to fracture. For I: A = (Q3)p-(Q2)n -(Q1)-(Q)m-, wherein Q is CH2 and m is 0, 1, or 2, or Q is OCH2 and m is 1, or Q is N(R')CH2 and m is 1, where R' is H or C1-C6 alkyl; Q1 is aryl or heteroaryl; Q2 is CH2 and n is 0, or 1, or Q2 is CH2O and n is 1, or Q2 is N(R') and n is 1, where R' is H or C1-C6 alkyl; Q3 is aryl or heteroaryl and p is 0 or 1; R' is C1-C6 alkyl, C3-C6 cycloalkyl or C3-C6 cycloalkyl substituted with C1-C6 alkyl; D is O or S; R2 is H or -NR3R4; R3, R6, and R7 = H or C1-C6 alkyl; R4 is H, C1-C6 alkyl, -C(O)R5, -C(O)OR5, -S(O)2R5; R5 is H, C1-C6 alkyl, or -NR6R7; Z = -(X)m-(X1), wherein X is C(R'')(R'''), wherein R'' is H or C1-C6 alkyl, R''' is H or C1-C6 alkyl, and m is 0, 1, or 2; and X1 is aryl, heteroaryl, or heterocyclyl. Although the methods of preparation are not claimed, 65 example prepns. of I and intermediates are included. Each of I in the Examples section bind with high affinity (IC50 < 10 μM) to the cathepsin K enzyme; for example, IC50 = 1-0.01 nM for (1S)-2,2-dimethyl-1-[[3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]methyl]propyl (1S)-1-[oxo[(1H-pyrazol-5-ylmethyl)amino]acetyl]pentylcarbamate. Inhibition results for 7 examples of I are tabulated for different cathepsins (human and/or rat B, H, K, L, S, V).

IT ***497947-96-3P***, (1R)-1-[1,1'-Biphenyl]-3-yl-2,2-dimethylpropyl [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]carbamate
497948-03-5P, (1S)-1-[1,1'-Biphenyl]-3-yl-2,2-dimethylpropyl [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]carbamate
497948-46-6P, (1S)-2,2-Dimethyl-1-(3-thien-2-ylphenyl)propyl [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]carbamate
497948-50-2P, (1R)-2,2-Dimethyl-1-(3-thien-2-ylphenyl)propyl

[(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]carbamate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of α-ketoamide derivs. as cathepsin K inhibitors useful against bone disorders such as osteoporosis)

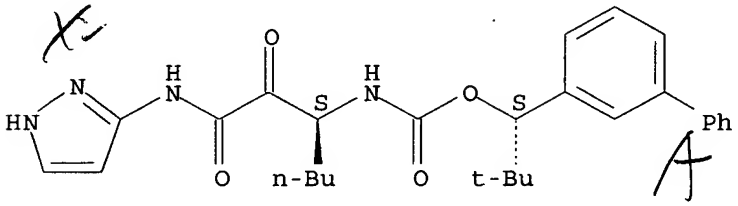
RN 497947-96-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1R)-1-[1,1'-biphenyl]-3-yl-2,2-dimethylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



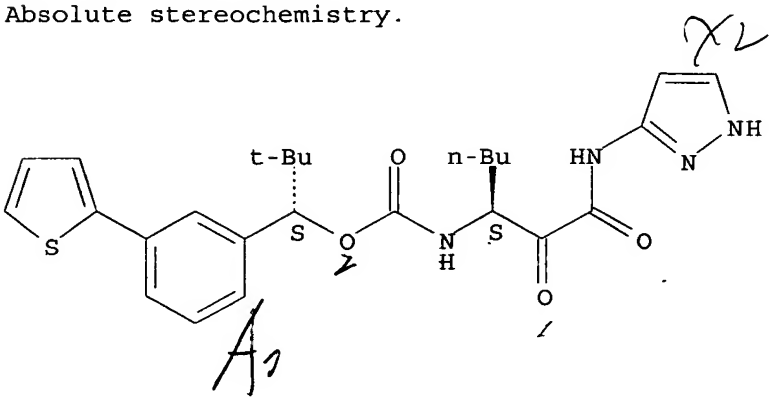
RN 497948-03-5 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1S)-1-[1,1'-biphenyl]-3-yl-2,2-dimethylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



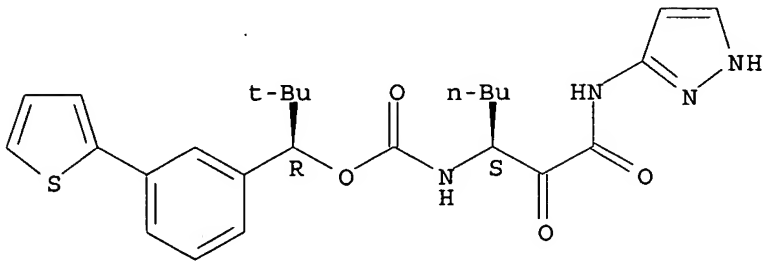
RN 497948-46-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1S)-2,2-dimethyl-1-[3-(2-thienyl)phenyl]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 497948-50-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[oxo(1H-pyrazol-3-ylamino)acetyl]pentyl]-, (1R)-2,2-dimethyl-1-[3-(2-thienyl)phenyl]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Powers, J	2001			US 6235929 B1	HCAPLUS
Sohda, T	1996			WO 9616079 A	HCAPLUS

L26 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:959797 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 139:2825
TITLE: Navigation Inside a Protease: Substrate Selection and Product Exit in the Tricorn Protease from Thermoplasma acidophilum
AUTHOR(S): Kim, Jeong-Sun; Groll, Michael; Musiol, Hans-Jurgen; Behrendt, Raymond; Kaiser, Markus; Moroder, Luis; Huber, Robert; Brandstetter, Hans
CORPORATE SOURCE: Max-Planck-Institut fur Biochemie, Planegg-Martinsried, D-82152, Germany
SOURCE: Journal of Molecular Biology (2002), 324(5), 1041-1050
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The proposed pathway and mechanism of substrate entry and product egress in the hexameric D3 sym. tricorn protease from Thermoplasma acidophilum were explored by crystallog. studies of ligand complexes and by structure-based mutagenesis. Obstruction of the pore within the 7-bladed β-propeller (β7) domain by alkylation or oxidation of an engineered double cysteine mutant strongly decreased enzymic activities. In line herewith, the crystal structure of the tricorn protease in complex with a trideca-peptide inhibitor modifying the catalytic Ser965 revealed part of the peptide trapped inside the channel of the β7 domain. The cysteine mutation widening the lumen of the 6-bladed β-propeller (β6) domain enhanced catalytic activity, which was restored to normal values after its alkylation. A charge reversal mutant at the putative anchor site of the substrate C terminus, R131E-R132E, drastically reduced the proteolytic activity. The complex crystal structure of a peptide inhibitor with a diketo group at the cleavage site mapped the substrate recognition site and confirmed the role of Arg131-Arg132 as an anchor site. Our results strongly suggest the wider β7 domain to serve as a

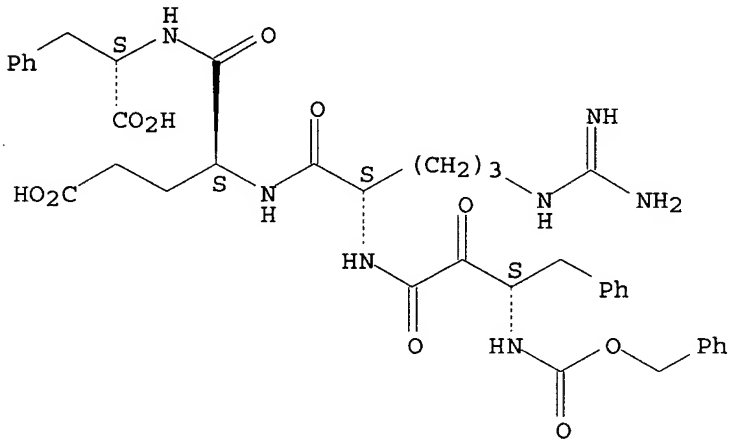
selective filter and guide for the substrate to the sequestered active site, while the narrower β6 domain routes the product to the surface. Moreover, we identified the role of Arg131-Arg132 in anchoring the substrate C terminus.

IT ***534615-52-6DP***, Inh3, complex with tricorn protease
RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(substrate selection and product exit in tricorn protease from Thermoplasma acidophilum)

RN 534615-52-6 HCAPLUS

CN L-Phenylalanine, N2-[(3S)-1,2-dioxo-4-phenyl-3-[[(phenylmethoxy)carbonyl]amino]butyl]-L-arginyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Baker, S	1997	269	440	J Mol Biol	HCAPLUS
Bochtler, M	2000	403	800	Nature	HCAPLUS
Bode, W	1989	8	3467	EMBO J	HCAPLUS
Brandstetter, H	2001	414	466	Nature	HCAPLUS
Brunger, A	1998	54	905	Acta Crystallog sect	MEDLINE
Cesar, J	2001	42	7099	Tetrahedron Letters	HCAPLUS
Esnouf, R	1997	15	132	J Mol Graph	HCAPLUS
Faber, H	1995	3	551	Structure	HCAPLUS
Fulop, V	1998	94	161	Cell	HCAPLUS
Fulop, V	2000	1	277	EMBO Rep	HCAPLUS
Goettig, P	2002	21	5343	EMBO J	HCAPLUS
Groll, M	1997	386	463	Nature	HCAPLUS
Groll, M	2000	7	1062	Nature Struct Biol	HCAPLUS
Harbeson, S	1994	37	2918	J Med Chem	HCAPLUS
Hiller, M	1996	273	1725	Science	HCAPLUS
Kraulis, P	1991	24	946	J Appl Crystallog	
Lowe, J	1995	268	533	Science	MEDLINE
Merritt, E	1997	227	505	Methods Enzymol	
Neer, J	1996	84	175	Cell	
Nicholls, A	1993	64	A166	Biophys J	

Otwinowski, Z	1997	276	307	Methods Enzymol	HCAPLUS
Rock, K	1994	78	761	Cell	HCAPLUS
Sommer, T	1997	11	1227	FASEB J	HCAPLUS
Sommer, T	1994	365	176	Nature	
Tamura, N	1998	95	637	Cell	HCAPLUS
Tamura, T	1996	398	101	FEBS Letters	HCAPLUS
Tamura, T	1996	274	1385	Science	HCAPLUS
Walz, J	1999	128	65	J Struct Biol	HCAPLUS
Walz, J	1997	1	59	Mol Cell	HCAPLUS

L26 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:90069 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 136:145200
TITLE: Novel peptides as ns3-serine protease inhibitors of hepatitis C virus
INVENTOR(S): Lim-Wilby, Marguerita; Levy, Odile E.; Brunck, Terrence K.
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008251	A2	20020131	WO 2001-US23169	20010719
WO 2002008251	A3	20030109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2418199	AA	20020131	CA 2001-2418199	20010719
US 2002068702	A1	20020606	US 2001-909164	20010719
EP 1301527	A2	20030416	EP 2001-955916	20010719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004504407	T2	20040212	JP 2002-514155	20010719

PRIORITY APPLN. INFO.: US 2000-220101P P 20000721
WO 2001-US23169 W 20010719

OTHER SOURCE(S): MARPAT 136:145200

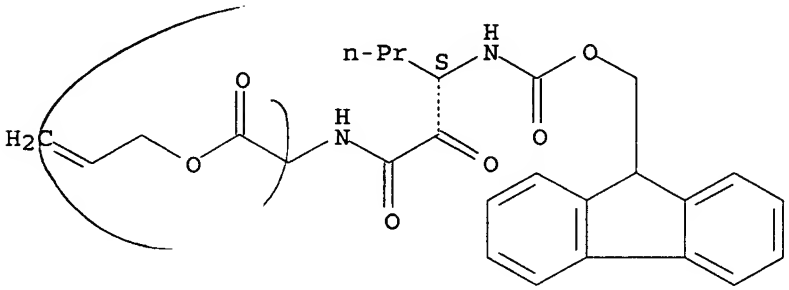
AB The present invention discloses novel peptide compds. containing eleven amino acid residues which have hepatitis C virus (HCV) protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such peptides as well as methods of using them to treat disorders associated with the HCV protease.

IT ***276888-38-1P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel peptides as ns3-serine protease inhibitors of hepatitis C virus and combination with other antiviral agents)

RN 276888-38-1 HCAPLUS

CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:90062 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 136:167698
TITLE: Preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus
INVENTOR(S): Saksena, Anil K.; Girijavallabhan, Viyyoor Moopil; Lovey, Raymond G.; Jao, Edwin E.; Bennett, Frank; McCormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Chan, Tin-Yau; Liu, Yi-Tsung; Zhu, Zhaoning; Njoroge, F. George; Arasappan, Ashok; Parekh, Tejal N.; Ganguly, Ashit K.; Chen, Kevin X.; Venkatraman, Srikanth; Vaccaro, Henry A.; Pinto, Patrick A.; Santhanam, Bama; Wu, Wanli; Hendrata, Siska; Huang, Yuhua; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.
PATENT ASSIGNEE(S): Schering Corporation, USA; Corvas International, Inc.
SOURCE: PCT Int. Appl., 536 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008244	A2	20020131	WO 2001-US22678	20010719
WO 2002008244	A3	20030619		
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CA 2410662	AA	20020131	CA 2001-2410662	20010719
AU 2001076988	A5	20020205	AU 2001-76988	20010719
BR 2001012540	A	20030624	BR 2001-12540	20010719
EP 1385870	A2	20040204	EP 2001-954764	20010719

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004504404	T2	20040212	JP 2002-514149		20010719
CN 1498224	A	20040519	CN 2001-813111		20010719
HU 200401730	A2	20041228	HU 2004-1730		20010719
NZ 523782	A	20051028	NZ 2001-523782		20010719
ZA 2002010312	A	20040329	ZA 2002-10312		20021219
NO 2003000272	A	20030321	NO 2003-272		20030120
PRIORITY APPLN. INFO.:			US 2000-220108P	P	20000721
			WO 2001-US22678	W	20010719

OTHER SOURCE(S): MARPAT 136:167698

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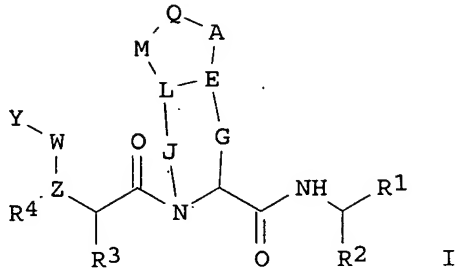

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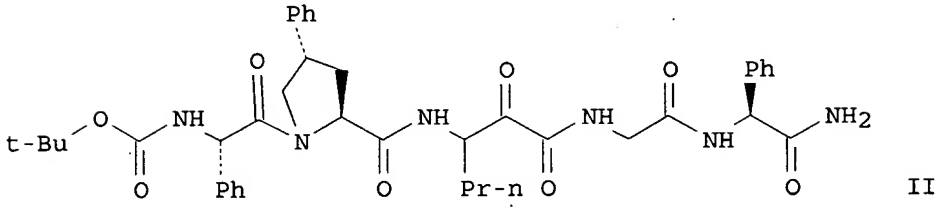
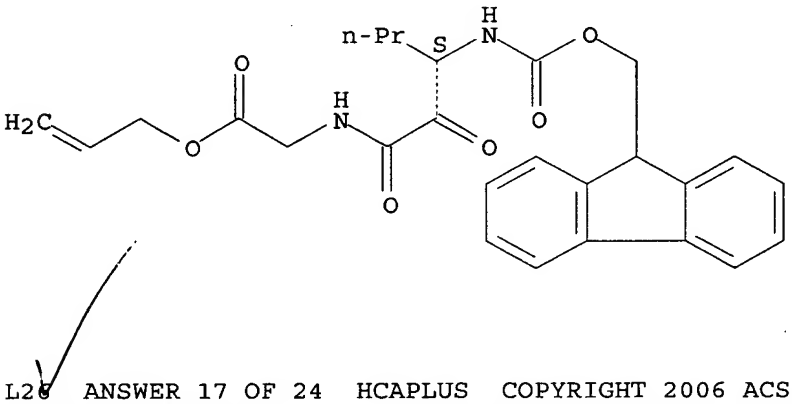


II

AB Peptides I were prepared wherein Y is alkyl, alkyl-aryl, heteroaryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkylheteroaryl, cycloalkyl, alkyloxy, alkylaryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy,, alkylamino, arylamino, alkylarylamino, arylamino, heteroarylamino, cycloalkylamino and heterocycloalkylamino; R1 is acyl, borate; Z is selected from O, N, CH or CR; W, Q, G, J, L, M independently maybe present or absent; W is C=O, C=S, C(=N-CN), or SO; Q is CH, N, P, alkylidene, O, amine,S, or SO; A is O, CH, alkylidene, amine, S, SO or bond; E is CH, N, alkylidene, or double bond; G is alkylidene; J is alkylidene, SO, NH, NR, O; L is CH, alkylidene, O, S or NR; M is O, NR,S, SO, alkylidene; p is 0 to 6; and R-R4 are independently selected from the group consisting of H; alkyl; alkenyl; cycloalkyl; heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, halogen; (cycloalkyl)alkyl and (heterocycloalkyl)alkyl, which have HCV protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such compds. as well as methods of using them to treat disorders associated with the HCV protease. Thus peptide II was prepared and tested as antiviral agent and NS3-serine protease inhibitors of hepatitis C virus with Ki ranges in category A = 1-100 nM; category B = 101-1,000 nM; category C > 1000 nM. Also disclosed is the use of I for the manufacture of a medicament for treating HCV, AIDS, and related disorders.

IT *276888-38-1P*
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)
RN 276888-38-1 HCAPLUS
CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:90007 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 136:151439
TITLE: Preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus
INVENTOR(S): Saksena, Anil K.; Girijavallabhan, Viyyoor Moopil; Bogen, Stephane L.; Lovey, Raymond G.; Jao, Edwin E.; Bennett, Frank; McCormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Liu, Yi-Tsung; Chan, Tin-Yau; Zhu, Zhaoning; Arasappan, Ashok; Chen, Kevin X.; Venkatraman, Srikanth; Parekh, Tejal N.; Pinto, Patrick A.; Santhanam, Bama; Njoroge, F. George; Ganguly, Ashit K.; Vaccaro, Henry A.; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.
PATENT ASSIGNEE(S): Schering Corporation, USA; Corvas International, Inc.
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008187	A1	20020131	WO 2001-US22813	20010719
WO 2002008187	C2	20030103		

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BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2410682	AA	20020131	CA 2001-2410682	20010719
US 2002160962	A1	20021031	US 2001-909012	20010719
EP 1303487	A1	20030423	EP 2001-959041	20010719
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BR 2001012666	A	20030610	BR 2001-12666	20010719
HU 200303358	A2	20040128	HU 2003-3358	20010719
JP 2004513881	T2	20040513	JP 2002-514094	20010719
NZ 523781	A	20041029	NZ 2001-523781	20010719
ZA 2002010311	A	20040319	ZA 2002-10311	20021219
NO 2003000271	A	20030318	NO 2003-271	20030120
US 2005176648	A1	20050811	US 2005-89192	20050324
PRIORITY APPLN. INFO.:			US 2000-220107P	P 20000721
			US 2001-909012	A3 20010719
			WO 2001-US22813	W 20010719

OTHER SOURCE(S): MARPAT 136:151439

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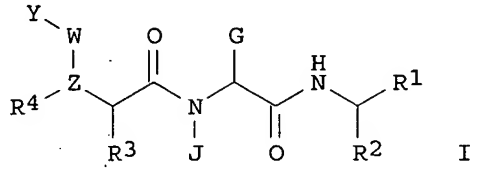

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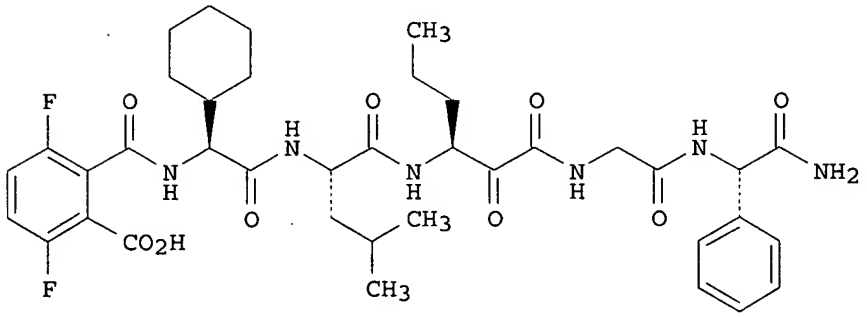


II

AB Novel peptides I [G, J, Y = independently H, alkyl, alkyl-aryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkoxy, alkyl-aryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkyl-arylamino, arylamino, heteroarylamino, cycloalkylamino, and heterocycloalkylamino; Z = O, N, CH; W = null, CO, CS, SO2; R1 = COR5, B(OR)2; R5 = H, OH, OR8, NR9R10, CF3, C2F5, C3F7, CF2R6, R6, COR7; R7 = H, OH, OR8, CHR9R10, NR9R10; R6, R8-10 = independently H, alkyl, aryl, heteroalkyl, cycloalkyl, arylalkyl, peptide derivative, etc.; R, R2-4 = independently H, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, etc.] and their pharmaceutically salts which have hepatitis C virus (HCV) protease inhibitory activity were prepared via solution or solid-phase peptide coupling methods. Thus, peptide II was prepared using solid-phase methods and showed a Ki value in the range of 0-100 nM for HCV protease inhibitory activity. This invention also

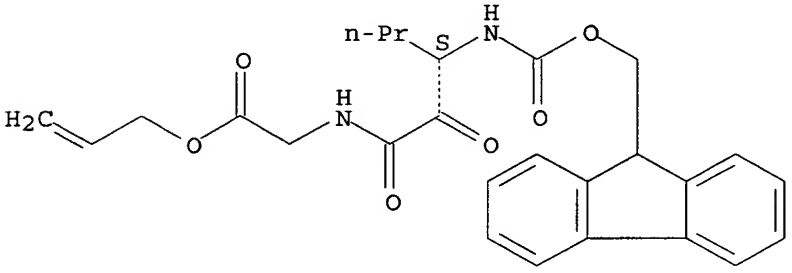
discloses pharmaceutical compns. comprising such compds. as well as methods of using them to treat disorders associated with the HCV protease.

IT *276888-38-1P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 276888-38-1 HCAPLUS

CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
F Hoffmann-La Roche Ag	1998			WO 9822496 A2	HCAPLUS
Hanson	1996			US 5488067 A	HCAPLUS
Powers	1996			US 5514694 A	HCAPLUS

L26 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:416971 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 135:19916
TITLE: Preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease
INVENTOR(S): Han, Wei
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040262	A1	20010607	WO 2000-US32677	20001201
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2390349	AA	20010607	CA 2000-2390349	20001201
US 2002123468	A1	20020905	US 2000-728653	20001201
US 6774212	B2	20040810		
EP 1252178	A1	20021030	EP 2000-983845	20001201

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR

JP 2003526634	T2	20030909	JP 2001-541017		20001201
PRIORITY APPLN. INFO.:			US 1999-168998P	P	19991203
			WO 2000-US32677	W	20001201

OTHER SOURCE(S): MARPAT 135:19916

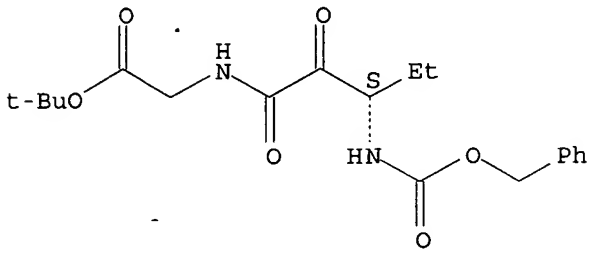
AB Keto amide and keto ester compds. R9-A6-A5-A4-A3-A2-NHCR1R2COCO-W-Q [W = NH or O; Q = substituted alkyl, alkenyl, or alkynyl or an amino acid residue; A2 is a bond, NHCH2CO which may be C-substituted, an amino acid residue, or NRCHRCO, where NRCHR represents tetrahydropyrrole-1,2-diyl which may be substituted at the 4- and 5-positions or hexahydroindole-1,2-diyl; A3 or A4 is a bond, NHCH2CO which may be C-substituted, or an amino acid residue; A5 or A6 is a bond or an amino acid residue; R1 = H, F, or substituted alkyl, alkenyl, alkynyl, aryl, or cycloalkyl; R2 = H, F, alkyl; R9 = S(O)R9a, SO2R9a, C(O)R9a, C(O)OR9a, C(O)NHR9a, alkyl-R9a, alkenyl-R9a, or alkynyl-R9a, where R9a = substituted alkyl, cycloalkyl, aryl, or heterocyclyl] or stereoisomeric forms or pharmaceutically acceptable salts were prepared as inhibitors of HCV NS3 protease. Thus, N-(2-pyrazinylcarbonyl)-L-leucyl-L-isoleucyl-3-cyclohexyl-L-alanyl-2-oxo-(3S)-3-aminopentanoylglycine was prepared by a multistep sequence which includes peptide coupling reactions in solution Compds. of the invention exhibit ki values of ≤60 μM, thereby confirming their utility as effective NS3 protease inhibitors.

IT ***342612-60-6P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

RN 342612-60-6 HCAPLUS

CN Glycine, N-[(3S)-1,2-dioxo-3-[[(phenylmethoxy)carbonyl]amino]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



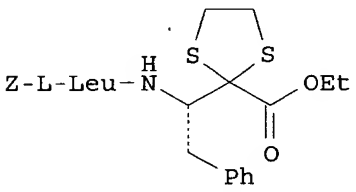
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Akzo Nobel Nv	1998			WO 9850420 A	HCAPLUS
Alkermes Inc	1995			WO 9500535 A	HCAPLUS
Bailey, M	1999			WO 9907734 A	HCAPLUS
Beecham Group Plc	1991			EP 0445467 A	HCAPLUS
Boehringer Ingelheim Ca	1998			WO 9829435 A	HCAPLUS
Cephalon Inc	1999			WO 9917790 A	HCAPLUS
Deininger, D	1998			WO 9817679 A	HCAPLUS
Georgia Tech Res Inst	1992			WO 9212140 A	HCAPLUS
Zaidan Hojin Biseibutsu	1991			EP 0423358 A	HCAPLUS

L26 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:366736 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 134:340711
TITLE: Preparation of tripeptide α-ketoamides as serine and cysteine protease inhibitors
INVENTOR(S): Powers, James C.
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. 5,650,508.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6235929	B1	20010522	US 1996-777354	19961227
US 5650508	A	19970722	US 1995-539944	19951006
PRIORITY APPLN. INFO.:			US 1991-815073	B1 19911227
			US 1993-118997	B1 19930909
			US 1994-246511	B1 19940520
			US 1995-539944	A2 19951006

OTHER SOURCE(S): MARPAT 134:340711
GI



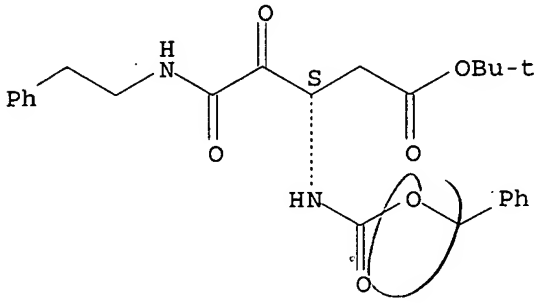
I

AB Tripeptide α-ketoamides M1-AA1-AA2-AA3-CONR3R4 [M1 = H, NH2CO, NH2CS, NH2SO2, XNHCO, X2NCO, XNHCS, X2NCS, XNHSO2, X2NSO2, XCO, XCS, XSO2, XO2C, XOCS; X = (un)substituted C1-10 alkyl or fluoroalkyl, 1-adamantyl, 9-fluorenyl, (un)substituted Ph or naphthyl; AA1 and AA2 = independently side-chain (un)blocked amino acid selected from alanine, valine, leucine, isoleucine, glycine, serine, aspartic acid, and glutamic acid; AA3 = aspartic or glutamic acid; R3 = alkyl or cycloalkyl substituted by Ph and optionally other substituents; R4 = H, alkyl or cycloalkyl which may have a Ph group and other substituents] were prepared as serine and cysteine protease inhibitors. Thus, condensation of protected peptidyl ketoester I (Z = PhCH2O2C) (prepared in 3 steps from Z-Leu-Phe-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH2 (R = Et, Pr, Bu, Bu-i, CH2Ph, CH2CH2Ph) gave peptidyl ketoamides Z-Leu-Phe-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with Ki = 8-73 μM and had half-lives in liver and plasma of >60.

IT ***208715-40-6P 208715-43-9P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide ketoamides as serine and cysteine protease

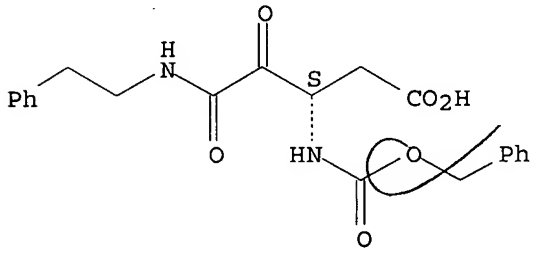
inhibitors)
RN 208715-40-6 HCAPLUS
CN Pentanoic acid, 4,5-dioxo-5-[(2-phenylethyl)amino]-3-[[(phenylmethoxy)carbonyl]amino]-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208715-43-9 HCAPLUS
CN Pentanoic acid, 4,5-dioxo-5-[(2-phenylethyl)amino]-3-[[(phenylmethoxy)carbonyl]amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Angelastro	1990	33	11	Journal of Medicinal	HCAPLUS
Anon	1986			EP 195212	HCAPLUS
Anon	1990			EP 363284	HCAPLUS
Anon	1992			WO 9212140	HCAPLUS
Bartas	1995			US 5444042	HCAPLUS
Burkhart	1988	29	3433	Tetrahedron Lett	HCAPLUS
Harbeson	1996			US 5541290	HCAPLUS
Hu	1990	281	271	Arch Biochem Biophys	HCAPLUS
Kolb	1996			US 5496927	HCAPLUS
Powers	1996			US 5514694	HCAPLUS
Powers	1997			US 5610297	HCAPLUS
Webb	1994			US 5371072	HCAPLUS
Webb	1997			US 5597804	HCAPLUS
Zhaozhao	1993	36	3472	Journal of Medicinal	

L26 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:115176 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 134:163332
TITLE: Preparation of peptidyl antipicornaviral compounds
INVENTOR(S): Dragovich, Peter Scott; Zhou, Ru; Webber, Stephen Evan; Prins, Thomas J.; Reich, Siegfried Heinz; Kephart, Susan E.; Rui, Yuanjin
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001010894	A2	20010215	WO 2000-US21061		20000803
WO 2001010894	A3	20010607			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2380647	AA	20010215	CA 2000-2380647		20000803
AU 2000065112	A5	20010305	AU 2000-65112		20000803
AU 779321	B2	20050120			
BR 2000012970	A	20020430	BR 2000-12970		20000803
EP 1206484	A2	20020522	EP 2000-952406		20000803
EP 1206484	B1	20041006			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
HU 200203108	A2	20021228	HU 2002-3108		20000803
JP 2003506457	T2	20030218	JP 2001-515702		20000803
US 6534530	B1	20030318	US 2000-631708		20000803
AT 278707	E	20041015	AT 2000-952406		20000803
PT 1206484	T	20050131	PT 2000-952406		20000803
ES 2230135	T3	20050501	ES 2000-952406		20000803
ZA 2002000881	A	20030204	ZA 2002-881		20020131
PRIORITY APPLN. INFO.:			US 1999-147373P	P	19990804
			WO 2000-US21061	W	20000803

OTHER SOURCE(S): MARPAT 134:163332

AB Peptides R4NHCR3R9CO-Y-CR2R8CONHCR7(COR1)CR5R6-Q [Y = NH, alkylimino, methylene, alkylmethylene, or O;R1 = substituted alkyl, cycloalkyl, heterocycloalkyl, aryl,heteroaryl, or acyl;R2, R8 = H, F, optionally substituted alkyl,cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;R3, R9 = H, optionally substituted alkyl,cycloalkyl, heterocycloalkyl, aryl, heteroaryl, hydroxy, thiol, or amino groups or alkoxy, aryloxy, etc.; R4 is a suitable organic moiety;R5, R6, R7 = H, F, or alkyl; m = 0 or 1; Q is a moiety comprising A1-CO-A4-(A3)p-(A2)m attached at A1, where m = 0 or 1, p = 0-5, A1 = CH or N; when m is 1 or p is not 0, A2, A3 = CR10R11, NR12, S, S(O), SO2, or O, where R10-R12 = H, alkyl; when p is not 0, A4 = = NR13, CR10R11, or O and when p is 0, A4 = NR13R14, CR10R11R12, or OR14, where R13 = H, alkyl, aryl, or acyl and R14 = H, alkyl, or aryl (with other provisos)] or their pharmaceutically acceptable salts, metabolites, or

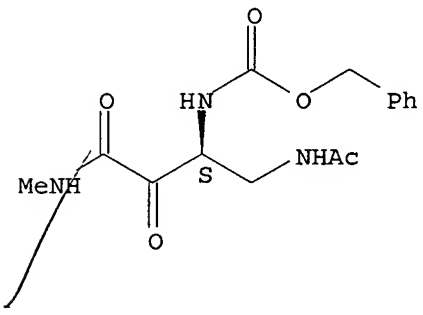
prodrugs were prepared as picornaviral 3C protease inhibitors. Thus, Cbz-L-Leu-L-Phe-L-(Tr-Gln)-CH2SMe (Cbz = benzyloxycarbonyl, Tr = trityl group) was prepared and showed Ki = 14 μM for inhibition of Rhinovirus 3C protease.

IT *325481-95-6P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptidyl antipicornaviral compds.)

RN 325481-95-6 HCAPLUS

CN Carbamic acid, [(1S)-1-[(acetylamino)methyl]-3-(methylamino)-2,3-dioxopropyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:421096 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 133:59100
TITLE: Methods for the synthesis of α-hydroxy-β-amino acid and amide derivatives
INVENTOR(S): Semple, Joseph E.; Levy, Odile E.
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035868	A2	20000622	WO 1999-US30267	19991216
WO 2000035868	A3	20010104		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6376649	B1	20020423	US 1998-216134	19981218
CA 2354476	AA	20000622	CA 1999-2354476	19991216
EP 1140854	A2	20011010	EP 1999-967427	19991216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002532466 T2 20021002 JP 2000-508130 19991216
PRIORITY APPLN. INFO.: US 1998-216134 A 19981218
WO 1999-US30267 W 19991216

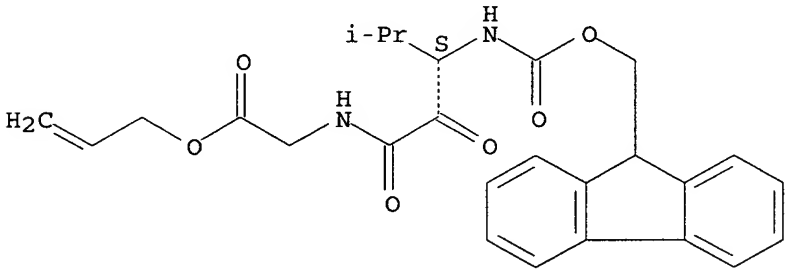
OTHER SOURCE(S): MARPAT 133:59100

AB Methods for the synthesis of α-hydroxy-β-amino acid and amide derivs. and α-ketoamide derivs. and novel derivs. made by these methods are provided. These methods involve reacting an N-terminally blocked (protected) aminoaldehyde with an isonitrile and a carboxylic acid to give an amino-α-acyloxy carboxamide. The acyloxy group may be removed to give the derivative Alternatively the protecting group is removed and acyl shift occurs to give the derivative These derivs. are useful in the synthesis of compds. such as peptidyl α-ketoamides and α-hydroxy-β-carboxylic acid and amide derivs. Thus, α-acyloxy-β-protected amino acid derivs. Boc-NHCH[(S)(CH2)3NHC(NH2):NNO2]CH(O2CR)CO-Gly-OEt (R = Fmoc-Pro, Alloc-Pro, Ac, Bz, COCH2CH2Ph) are among the compds. prepared

IT ***276888-37-0 276888-38-1 276888-39-2 276888-40-5 276888-41-6 276888-42-7 276888-43-8***
RL: RCT (Reactant); RACT (Reactant or reagent)
(methods for synthesis of α-hydroxy-β-amino acid and amide derivs.)

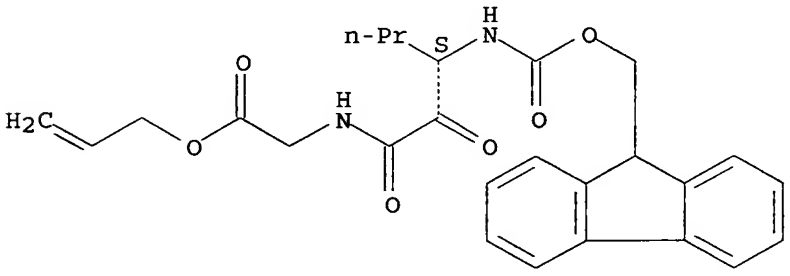
RN 276888-37-0 HCAPLUS
CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-4-methyl-1,2-dioxopentyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



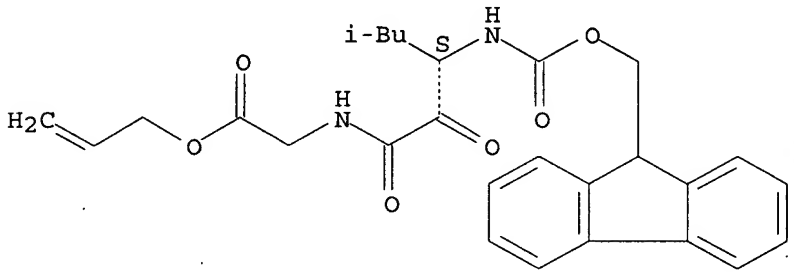
RN 276888-38-1 HCAPLUS
CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



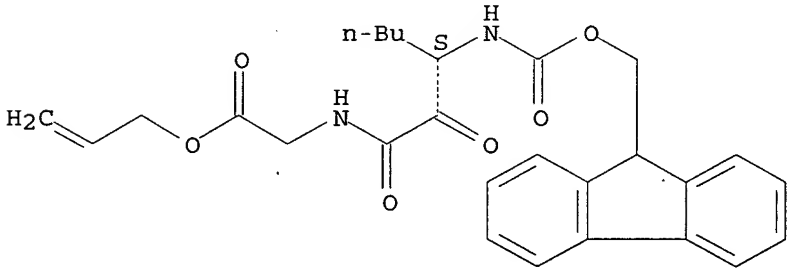
RN 276888-39-2 HCAPLUS
CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-5-methyl-1,2-dioxohexyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



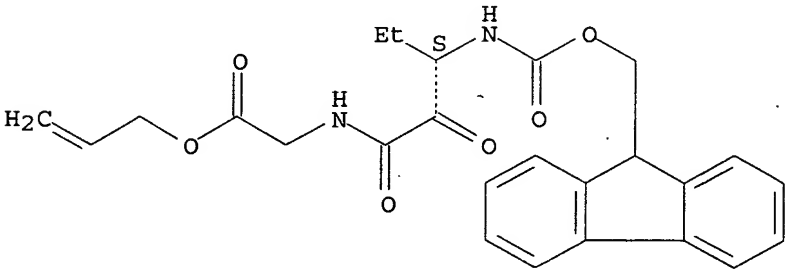
RN 276888-40-5 HCAPLUS
CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxoheptyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 276888-41-6 HCAPLUS
CN Glycine, N-[(3S)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,2-dioxopentyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

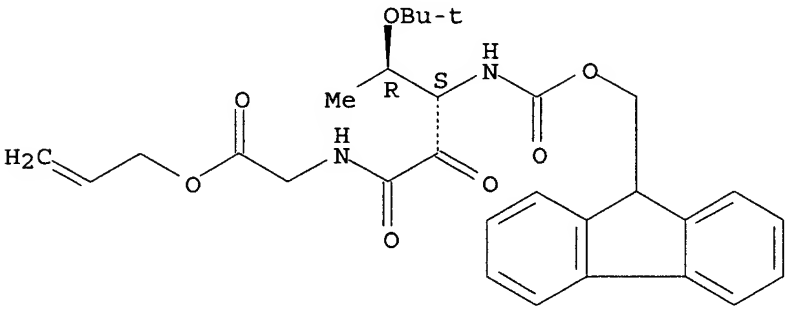
Absolute stereochemistry.



RN 276888-42-7 HCAPLUS

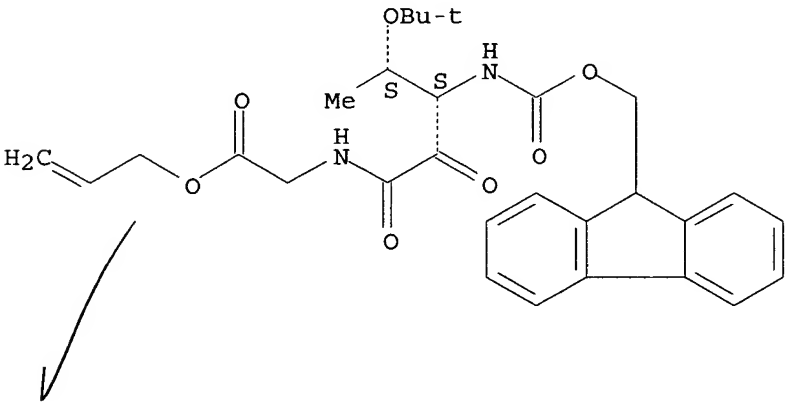
CN Glycine, N-[3,5-dideoxy-4-O-(1,1-dimethylethyl)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-D-threo-2-pentulosonoyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 276888-43-8 HCAPLUS
CN Glycine, N-[3,5-dideoxy-4-O-(1,1-dimethylethyl)-3-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-L-erythro-2-pentulosonoyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

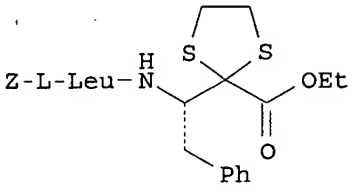


L26 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:397812 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 129:54609
TITLE: Preparation of peptide α-ketoamides as serine and cysteine protease inhibitors
INVENTOR(S): Powers, James C.
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA
SOURCE: U.S., 25 pp., Cont.-in-part of U. S. 5,650,508. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763576	A	19980609	US 1996-777208	19961227

US 5650508	A	19970722	US 1995-539944	19951006
PRIORITY APPLN. INFO.:			US 1995-539944	A2 19951006
			US 1991-815073	B1 19911227
			US 1993-118997	B1 19930909
			US 1994-246511	B1 19940520

OTHER SOURCE(S): MARPAT 129:54609
GI



I

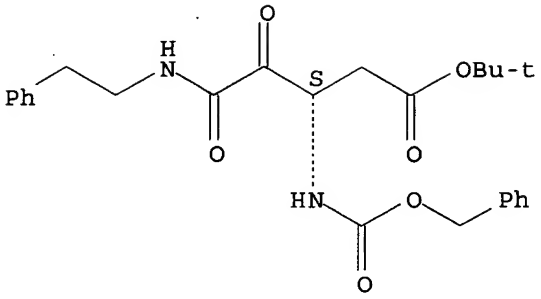
AB Di-, tri-, and tetrapeptide α-ketoamides M1-AA-NHCHR2COCONR3R4, M1-AA2-AA-CONR3R4, M1-AA1-AA2-AA3-CONR3R4, and M1-AA1-AA2-AA3-AA4-CONR3R4 [M1 = H, NH2CO, NH2CS, NH2SO2, XNHCO, X2NCO, XNHCS, X2NCS, XNHSO2, X2NSO2, XCO, XCS, XSO2, XO2C, XOCS; X = (un)substituted C1-10 alkyl, (un)substituted C1-10 fluoroalkyl, 1-adamantyl, 9-fluorenyl, (un)substituted Ph, (un)substituted naphthyl; AA, AA1, AA2, AA3, AA4 = independently side-chain (un)blocked amino acid; R2 = C1-8 (un)branched alkyl, C1-8 (un)branched cycloalkyl, C1-8 (un)branched fluoroalkyl; R3, R4 = independently H, C1-20 alkyl, C3-20 cycloalkyl, C1-20 arylalkyl, C1-10 heterocycloalkyl] are useful for selectively inhibiting serine proteases, selectively inhibiting cysteine proteases, generally inhibiting all serine proteases, and generally inhibiting all cysteine proteases. Thus, condensation of protected peptidyl ketoester I (Z = PhCH2O2C) (prepared in 3 steps from Z-Phe-Leu-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH2 (R = Et, Pr, Bu, CH2CHMe2, CH2Ph, CH2CH2Ph) gave peptidyl ketoamides Z-Phe-Leu-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with Ki = 8-73 mM, and had half-lives in liver and plasma of >60.

IT ***208715-40-6P 208715-43-9P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide ketoamides as serine and cysteine protease inhibitors)

RN 208715-40-6 HCAPLUS

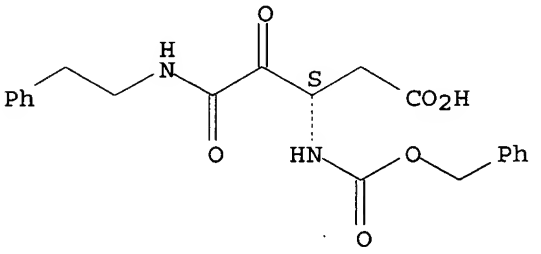
CN Pentanoic acid, 4,5-dioxo-5-[(2-phenylethyl)amino]-3-[[(phenylmethoxy)carbonyl]amino]-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208715-43-9 HCAPLUS
CN Pentanoic acid, 4,5-dioxo-5-[(2-phenylethyl)amino]-3-[[(phenylmethoxy)carbonyl]amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1990			EP 363284	HCAPLUS
Conforth	1953		93	Journal of the Chemi	
Harbeson	1996			US 5541290	HCAPLUS
Kolb	1996			US 5496927	HCAPLUS
Webb	1994			US 5371072	HCAPLUS
Webb	1997			US 5597804	HCAPLUS

L26 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:26310 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 128:35014
TITLE: Synthesis of the Cyclic Peptidic Protease Inhibitor Eurystatin A Using Acyl Cyano Phosphorane Methodology
AUTHOR(S): Wasserman, Harry H.; Petersen, Anders K.
CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA
SOURCE: Journal of Organic Chemistry (1997), 62(26), 8972-8973
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:35014
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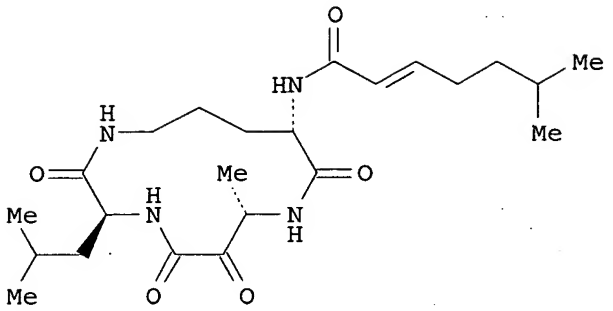


I

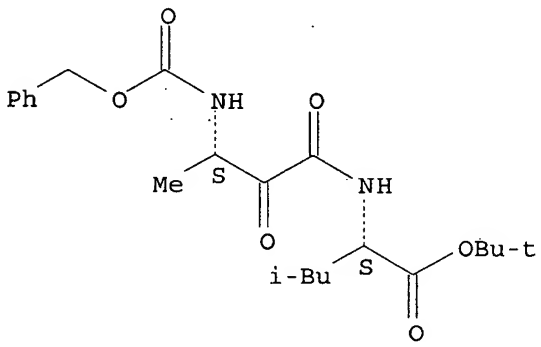
AB A synthesis of the cyclic protease inhibitor eurystatin A (I) was accomplished by two different routes, involving α,β-diketo nitriles obtained by oxidation of the corresponding acyl cyano phosphoranes. Coupling with leucine tert-Bu ester furnished the key α-keto amide functionality found in the natural product.

IT ***199467-17-9P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclopeptide protease inhibitor eurystatin A using acyl cyano phosphorane methodol.)

RN 199467-17-9 HCAPLUS

CN L-Leucine, N-[(3S)-1,2-dioxo-3-[[(phenylmethoxy)carbonyl]amino]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Aoyagi, T	1991	44	949	J Antibiot	HCAPLUS
Brady, S	1987	52	764	J Org Chem	HCAPLUS
Carballeira, N	1986	51	2751	J Org Chem	HCAPLUS
Carpino, L	1972	37	3404	J Org Chem	HCAPLUS
Corey, E	1975		2647	Tetrahedron Lett	HCAPLUS
Fusetani, N	1990	112	7053	J Am Chem Soc	HCAPLUS
Fusetani, N	1991	113	7811	J Am Chem Soc	HCAPLUS
Greco, M	1996	6	2947	BioMed Chem Lett	HCAPLUS

Gunasekera, S	1994	57	79	J Nat Prod	HCAPLUS
Hagihara, M	1992	114	6570	J Am Chem Soc	HCAPLUS
Hirschmann, R	1996	37	5637	Tetrahedron Lett	HCAPLUS
Johnson, A	1993			Ylides and Imines of	
Kamei, H	1992	60	377	Japan J Pharmacol	HCAPLUS
Kobayashi, J	1991	113	7812	J Am Chem Soc	HCAPLUS
Nagai, M	1991	44	956	J Antibiot	HCAPLUS
Rappe, C	1973	53	123	Organic Syntheses	HCAPLUS
Schmidt, U	1994		1003	J Chem Soc, Chem Com	HCAPLUS
Shioiri, T	1972	94	6203	J Am Chem Soc	HCAPLUS
Suzuki, K	1994	47	982	J Antibiot	HCAPLUS
Toda, S	1992	45	1573	J Antibiot	HCAPLUS
Toda, S	1992	45	1580	J Antibiot	HCAPLUS
Tsuda, M	1996	49	281	J Antibiot	HCAPLUS
Wasserman, H	1994	59	4364	J Org Chem	HCAPLUS
Wasserman, H	1997	38	953	Tetrahedron Lett	HCAPLUS
Wipf, P	1993	58	5592	J Org Chem	HCAPLUS
Wipf, P	1992	33	4275	Tetrahedron Lett	HCAPLUS

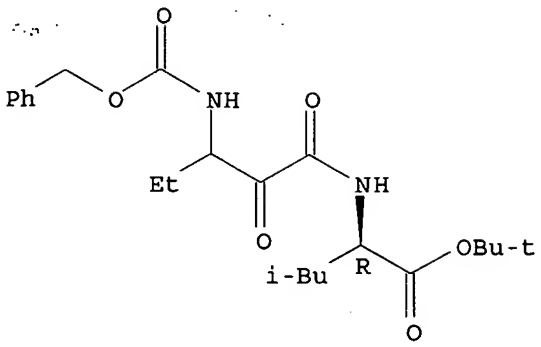
L26 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:592181 HCAPLUS <<LOGINID::20061206>>
DOCUMENT NUMBER: 125:295861
TITLE: Poststatin, a new inhibitor of prolyl endopeptidase. VI. Endopeptidase inhibitory activity of poststatin analogs containing pyrrolidine ring
AUTHOR(S): Tsuda, Makoto; Muraoka, Yasuhiko; Someno, Tetsuya; Nagai, Machiko; Aoyagi, Takaaki; Takeuchi, Tomio
CORPORATE SOURCE: Inst. Microbial Chem., Tokyo, 141, Japan
SOURCE: Journal of Antibiotics (1996), 49(9), 900-908
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several pyrrolidine-containing analogs of poststatin were synthesized and examined for their inhibitory activity against prolyl endopeptidase and cathepsin B in vitro. Replacement of the postine residue with 2-oxo-2-(2-pyrrolidinyl)acetic acid increased the selectivity and inhibitory activity against prolyl endopeptidase. benzyloxycarbonyl-L-phenylalanyl-(S)-2-oxo-2-(2-pyrrolidinyl)acetyl-D-phenylalanine was about 46 times as active to prolyl endopeptidase as natural poststatin.

IT ***182758-62-9P***
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(endopeptidase inhibitory activity of poststatin analogs containing pyrrolidine ring and their preparation)

RN 182758-62-9 HCAPLUS
CN D-Leucine, N-[1,2-dioxo-3-[[(phenylmethoxy)carbonyl]amino]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'MARPAT' ENTERED AT 17:05:26 ON 06 DEC 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE CONTENT: 1961-PRESENT VOL 145 ISS 22 (20061201/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US  20060234956 19 OCT 2006
DE 102005016345 12 OCT 2006
EP      1710237 11 OCT 2006
JP   2006282618 19 OCT 2006
WO   2006108879 19 OCT 2006
GB      2424583 04 OCT 2006
FR      2884252 13 OCT 2006
RU      2284857 10 OCT 2006
CA      2500558 10 SEP 2006

Expanded G-group definition display now available.

=> d que l43
L1              STR
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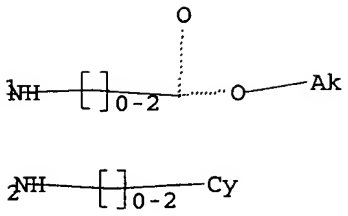

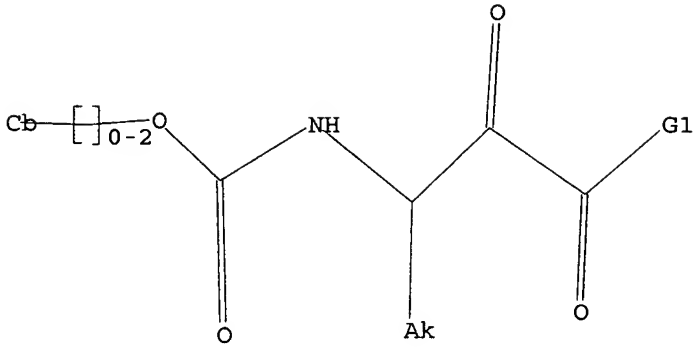

G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

L2 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2004-501636/AP

L3 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (WO2003-US1271/AP OR WO2003-US 1271/PRN)

L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US2002-349812P/PRN

L5 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4)

L6 193 SEA FILE=REGISTRY ABB=ON PLU=ON (103-63-9/BI OR 10445-91-7/BI OR 108-94-1/BI OR 109364-33-2/BI OR 110-91-8/BI OR 1191-95-3/BI OR 120-92-3/BI OR 131403-16-2/BI OR 1450-85-7/BI OR 1462-37-9/BI OR 14924-53-9/BI OR 15159-40-7/BI OR 16269-66-2/BI OR 16640-68-9/BI OR 16889-21-7/BI OR 1722-12-9/BI OR 17452-09-4/BI OR 17452-31-2/BI OR 175203-08-4/BI OR 1820-80-0/BI OR 196934-28-8/BI OR 2015-57-8/BI OR 21754-55-2/BI OR 21872-33-3/BI OR 2389-45-9/BI OR 24255-23-0/BI OR 2627-86-3/BI OR 3034-53-5/BI OR 3099-31-8/BI OR 3731-52-0/BI OR 3779-29-1/BI OR 3844-54-0/BI OR 3884-32-0/BI OR 3886-69-9/BI OR 3934-20-1/BI OR 39608-30-5/BI OR 433219-87-5/BI OR 4415-73-0/BI OR 459-46-1/BI OR 4630-80-2/BI OR 497946-73-3/BI OR 497946-74-4/BI OR 5217-04-9/BI OR 52857-42-8/BI OR 54314-84-0/BI OR 568590-60-3/BI OR 568590-61-4/BI OR 568590-62-5/BI OR 568590-63-6/BI OR 568590-64-7/BI OR 568590-65-8/BI OR 568590-66-9/BI OR 568590-67-0/BI OR 568590-68-1/BI OR 568590-69-2/BI OR 568590-70-5/BI OR 568590-71-6/BI OR 568590-72-7/BI OR 568590-73-8/BI OR 568590-74-9/BI OR 568590-75-0/BI OR 568590-77-2/BI OR 568590-78-3/BI OR 568590-79-4/BI OR 568590-80-7/BI OR 568590-81-8/BI OR 568590-82-9/BI OR 568590-83-0/BI OR 568590-84-1/BI OR 568590-85-2/BI OR 568590-86-3/BI OR 568590-87-4/BI OR 568590-88-5/BI OR 568590-89-6/BI OR 568590-90-9/BI OR 568590-91-0/BI OR 568590-92-1/BI OR 568590-93-2/BI OR 568590-94-3/BI OR 568590-95-4/BI OR 568590-96-5/BI OR 568590-97-6/BI OR 568590-98-7/BI OR 568590-99-8/BI OR

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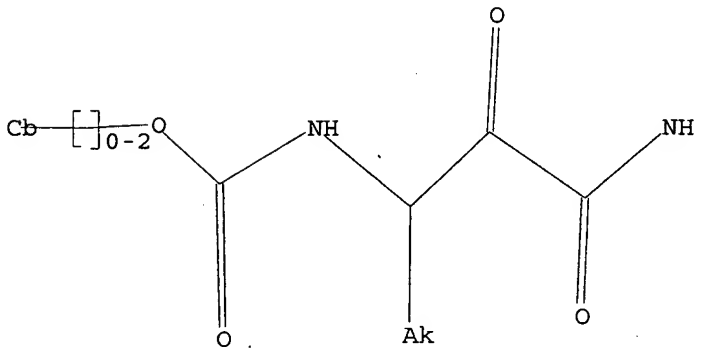
L8 38 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND L7
L10 STR



Structure attributes must be viewed using STN Express query preparation.

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L14 38 SEA FILE=REGISTRY ABB=ON PLU=ON (L8 OR L13)
L17 10 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L7
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L19 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L14
L20 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L21 25 SEA FILE=HCAPLUS ABB=ON PLU=ON (L18 OR L19 OR L20)
L22 25 SEA FILE=HCAPLUS ABB=ON PLU=ON (L21 OR L5)
L23 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 NOT L5
L24 25 SEA FILE=HCAPLUS ABB=ON PLU=ON L12
L25 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 NOT L5
L26 24 SEA FILE=HCAPLUS ABB=ON PLU=ON (L23 OR L25)
L41 39 SEA FILE=MARPAT SSS FUL L1
L42 30 SEA FILE=MARPAT ABB=ON PLU=ON L41/COM
L43 28 SEA FILE=MARPAT ABB=ON PLU=ON L42 NOT L26

=> d ibib abs qhit 143 tot

L43 ANSWER 1 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 145:117363 MARPAT <<LOGINID::20061206>>
TITLE: Use of sphingosine-1-phosphate (S1P) receptor agonists for the treatment of hepatitis C virus (HCV) disorders
INVENTOR(S): Brinkmann, Volker; Feutren, Gilles
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006072562	A1	20060713	WO 2006-EP3	20060102

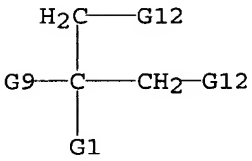
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-20 20050104

AB S1P receptor agonists are useful for the treatment of hepatitis C or chronic hepatitis C (HCV).

MSTR 1



G1 = 6

G2—G3—G4—G6
6

G2 = 292

G43=N—OH
292

G3 = NH
G7 = alkoxycarbonylamino / alkylcarbonyloxy <containing 1-20 C> (opt. substd. by Ph) / OH
G43 = carbon chain <containing 1-29 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by G7)
Patent location: claim 6
Note: or pharmaceutically acceptable salts
Note: substitution is restricted

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:350400 MARPAT <<LOGINID::20061206>>
TITLE: N-Ethyl hydroxyethylamines and their preparation, pharmaceutical compositions, β-secretase activity and use for treatment of CNS conditions
INVENTOR(S): Kleinman, Edward Fox; Murray, John Charles
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006033000	A2	20060330	WO 2005-IB2878	20050909
WO 2006033000	A3	20060518		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-611685P 20040921
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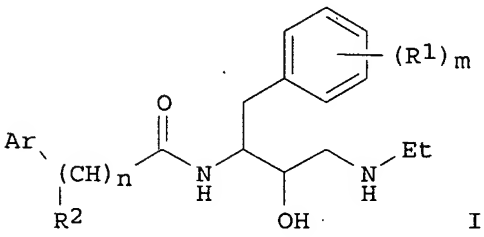

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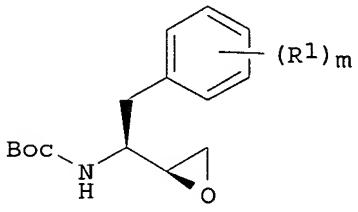
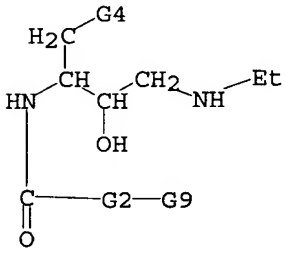


II

AB An N-Et hydroxyethylamine useful in treating CNS conditions, including neurodegenerative ones such as Alzheimer's disease, is disclosed. Compds. of formula I wherein n and m are independently 0, 1, 2 or 3; each R1 is independently H, halo, SH, NH2, (un)substituted C1-6 alkyl(oxy), (un)substituted S(C1-6 alkyl), (un)substituted NH(C1-6 alkyl), (un)substituted N(C1-6 alkyl)2, (un)substituted NHCO2(C1-6 alkyl), (un)substituted NHSO2(C1-6 alkyl), (un)substituted CONH(C1-6 alkyl), (un)substituted CON(C1-6 alkyl)2, C6-10 aryl, or 5- to 12-membered heteroaryl; R2 is H, C1-6 alkyl, (CH2)0-5(C6-10 aryl), and (CH2)0-5(5- to 12-membered)heteroaryl; Ar is (un)substituted C6-10 aryl, (un)substituted 5- to 12-membered heteroaryl, (un)substituted CO(C1-10 alkyl),

(un)substituted CO(C1-6 alkyl)O(C1-6 alkyl), (un)substituted CO(C1-6 alkyl)S(C1-6 alkyl), or (un)substituted CO(C3-8 cycloalkyl), etc.; with the exception of (1S,2R)-N-[1-(3,5-difluorobenzyl)-3-(ethylamino)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide; are claimed in this invention. Compds. of formula I can be prepared by ring opening of epoxides II; the resulting halohydrins were deprotected and the free amine underwent acylation with carboxylic acids to give the halo hydroxy amides, which reacted with methoxypropene to give acetonides, which reacted with ethylamine to give compds. of formula I. The invention compds. were evaluated for their β-secretase inhibitory activity (no data). No specific examples are cited, but a preferred general formula is given.

MSTR 1



G2 = bond
G4 = Ph (opt. substd. by (1-3) G5)
G9 = 169

C(O)—G13
169

G13 = alkyl <containing 1-10 C>
(opt. substd. by (1-3) G14)
G14 = 195

HN——C(O)—G26
195

G26 = 296

O——G28
296

G28 = Ph
Patent location: claim 1
Note: additional oxo and ring formation also claimed
Note: substitution is restricted
Note: additional substitution also claimed

Shiao 10/501636

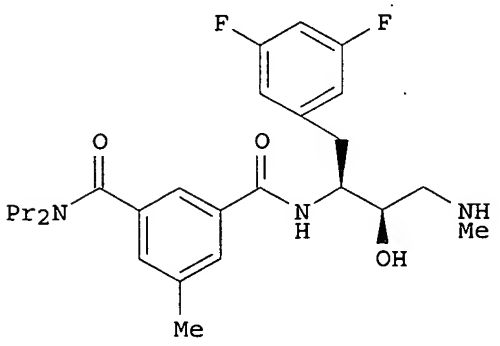
L43 ANSWER 3 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:350399 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of N-acyl-1-benzyl-2-hydroxy-N'-methyl-1,3-propanediamines useful in treating CNS conditions
INVENTOR(S): Kleinman, Edward Fox; Murray, John Charles
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006032999	A1	20060330	WO 2005-IB2877	20050909

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

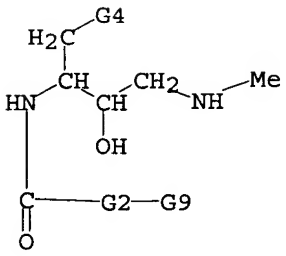
PRIORITY APPLN. INFO.: US 2004-611777P 20040921
GI



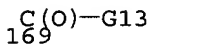
I

AB The invention relates to N-methylethanolamine derivs. R2(CHR1)0-3CONHCH(CH2Ar)CH(OH)CH2NHMe [Ar is Ph which may be substituted by 1-3 groups halogen, OH, CN, SH, NH2, alkyl, alkoxy, alkylthio, alkylamino, aryl, heteroaryl, etc.; R1 is H, alkyl, (hetero)aryl(CH2)0-5; R2 is (hetero)aryl, alkanoyl, cycloalkylcarbonyl, etc.] which are useful in treating CNS conditions, including Alzheimer's disease. Thus, compound I was prepared by a multistep procedure starting with reaction of (1R,2S)-[2-(3,5-difluorophenyl)-1-oxiranylethyl]carbamic acid tert-Bu ester with NaI.

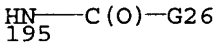
MSTR 1



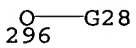
G2 = bond
G4 = Ph (opt. substd. by (1-3) G5)
G9 = 169



G13 = alkyl <containing 1-10 C>
(opt. substd. by (1-3) G14)
G14 = 195



G26 = 296



G28 = Ph
Patent location: claim 1
Note: additional oxo and ring formation also claimed
Note: substitution is restricted
Note: additional substitution also claimed

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 143:416305 MARPAT <<LOGINID::20061206>>
TITLE: Bone densifying agent characterized by use of cathepsin K inhibitor with PTH
INVENTOR(S): Ochi, Yasuo; Tanaka, Makoto; Kawada, Naoki; Yamada, Hiroyuki; Mori, Hiroshi; Kayasuga, Ryouji
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005102381	A1	20051103	WO 2005-JP7767	20050425

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2004-129454 20040426

AB To provide a bone densifying agent characterized by use of a cathepsin K inhibitor in combination with a PTH, there is provided a bone densifying agent characterized by use of a cathepsin K inhibitor as a medicine for bone resorption inhibition in combination with a PTH as a medicine for osteogenesis acceleration. This bone densifying agent is useful for the treatment of osteoporosis, bone fracture, arthritis, arthrorheumatism, osteoarthritis, hypercalcemia, osteometastasis of carcinoma, periodontal disease, Paget's disease of bone and other bone metabolic diseases. For example, the effect of oral administration of a cathepsin K inhibitor N-[3-[(2Z)-2-(3-methyl-1,3-thiazolidin-2-ylidene)hydrazino]-2,3-dioxo-1-tetrahydro-2H-pyran-4-ylpropyl]cycloheptanecarboxamide hydrochloride in combination with injection of human PTH (1-34) on bone d. in ovariectomized osteoporosis model rats was examined

MSTR 1

G24—G26
6

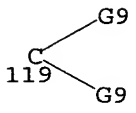
G1 = 155

C(O)-G39
155

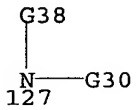
G9 = alkyl <containing 1-8 C> (opt. substd.)
G24 = 5

G1—G72
4 5

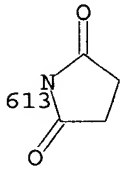
G25 = 119



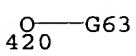
G26 = 127



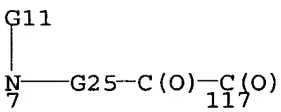
G30 = 613



G39 = 420



G63 = cyclopentyl
G72 = 7-4 117-6



Patent location: claim 3
Note: or salts, N-oxides, solvates or prodrugs
Note: additional ring formation also claimed

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:266775 MARPAT <<LOGINID::20061206>>
TITLE: Drug containing chymase inhibitor as the active ingredient
INVENTOR(S): Urata, Hidenori; Hase, Naoki; Tsuchiya, Naoki
PATENT ASSIGNEE(S): Teijin Pharma Limited, Japan
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018672	A1	20050303	WO 2004-JP12335	20040820
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266536	A1	20050303	AU 2004-266536	20040820
CA 2536435	AA	20050303	CA 2004-2536435	20040820
EP 1666067	A1	20060607	EP 2004-772291	20040820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871029	A	20061129	CN 2004-80030767	20040820
PRIORITY APPLN. INFO.:			JP 2003-298639	20030822
			WO 2004-JP12335	20040820

AB Disclosed is an agent for improving abnormal glucose tolerance or a preventive and/or a remedy for diseases caused by abnormal glucose tolerance containing a chymase inhibitor as the active ingredient. Examples of the diseases caused by abnormal glucose tolerance include diabetes and/or complications of diabetes. Examples of the complications of diabetes include diabetic nephropathy, diabetic retinopathy, diabetic peripheral neuropathy, hyperinsulinemia, insulin resistance syndrome, arteriosclerosis, acute coronary syndrome, arteriosclerosis obliterans, vasculitis, brain infarction, hypertension, renal insufficiency, neuropathy, nephritis, renal aneurysm, renal infarction, obesity and so on. Claimed chymase inhibitors include 4-[1-[(3-indolyl)methyl]benzimidazol-2-ylthio]butanoic acid and 2-[2-[5-amino-2-(4-fluorophenyl)-6-oxo-1,6-dihydropyrimidin-1-yl]acetamido]-3-phenylpropionylbenzoxazol-5-carboxylic acid Me ester.

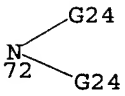
MSTR 3

G10—G35
88

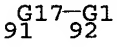
G7 = Ph (opt. substd.)
G10 = 128

HN——G16
128

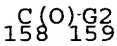
G14 = 72



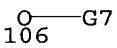
G16 = 91



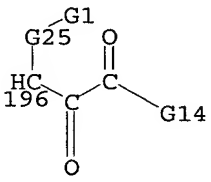
G17 = 158-128 159-92



G18 = 106



G21 = (0-3) CH2
G24 = Ph (opt. substd.)
G25 = alkylene (opt. substd. by 1 or more G26)
G35 = 196



Derivative: or pharmacologically acceptable salts
Patent location: claim 21

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:27657 MARPAT <<LOGINID::20061206>>
TITLE: Bis(dihydroxyaryl) compounds, pharmaceutical compositions containing them, and methods for the treatment of amyloid diseases and synucleinopathies such as Alzheimer's disease, type 2 diabetes, and Parkinson's disease.
INVENTOR(S): Snow, Alan D.; Nguyen, Beth P.; Castillo, Gerardo M.; Sanders, Virginia J.; Lake, Thomas P.; Larsen, Lesley; Weavers, Rex T.; Lorimer, Stephen D.; Larsen, David S.; Coffen, David L.

PATENT ASSIGNEE(S): Proteotech, Inc., USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101927	A1	20031211	WO 2003-US17288	20030530
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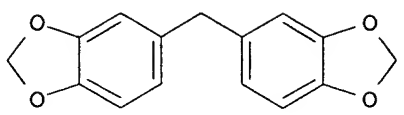
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2486869	AA	20031211	CA 2003-2486869	20030530
AU 2003249678	A1	20031219	AU 2003-249678	20030530
US 2004127555	A1	20040701	US 2003-452851	20030530
EP 1511710	A1	20050309	EP 2003-756343	20030530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005531596	T2	20051020	JP 2004-509622	20030530

PRIORITY APPLN. INFO.: US 2002-385144P 20020531
US 2002-409100P 20020909
US 2002-412272P 20020920
US 2002-435880P 20021220
US 2003-463104P 20030414
WO 2003-US17288 20030530

GI



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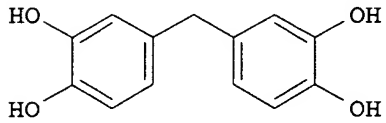
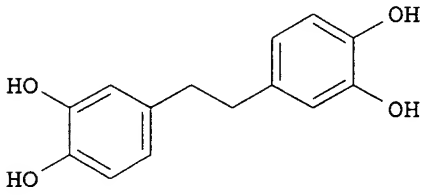


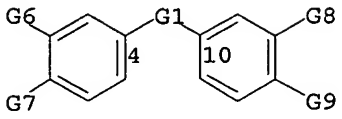
II



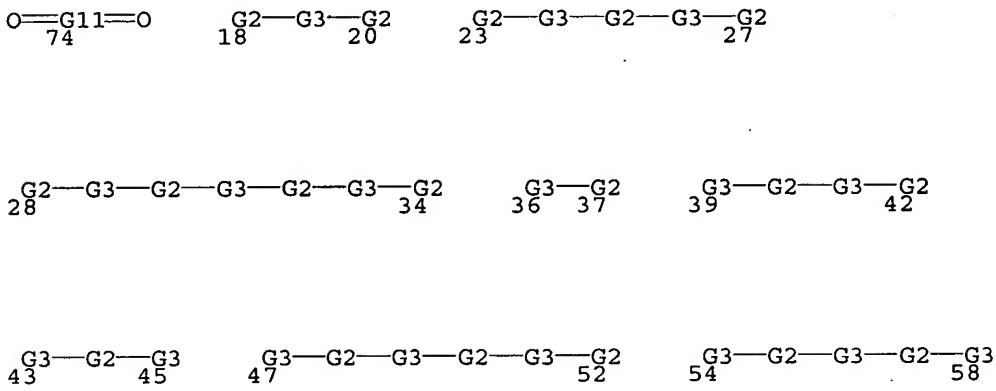
III

AB Bis- and tris(dihydroxyaryl) compds. and their methylenedioxy analogs and pharmaceutically acceptable esters are disclosed. The claimed compds. include (1) bis(diphenols) 3,4-(HO)2C6H3-R-C6H3(OH)2-3,4 [R = optionally modified/substituted C1-10 alkylene], (2) 86 specifically named compds., and (3) the methylenedioxy analogs and pharmaceutically acceptable esters of the preceding, and (4) pharmaceutically acceptable salts of all of these compds. Also disclosed are (1) synthesis of the compds., (2) pharmaceutical compns. containing them, (3) their use in the treatment of amyloid diseases, especially (a) Aβ amyloidosis (such as observed in Alzheimer's disease), (b) IAPP amyloidosis (such as observed in type 2 diabetes), and (c) synucleinopathies (such as observed in Parkinson's disease), as well as (4) the manufacture of medicaments for such treatments. Examples include 24 synthetic prepns., 3 biol. studies employing multiple assays, and a large listing of actual and prophetic example compds. For instance, Grignard reaction of piperonal with 3,4-(methylenedioxy)phenylmagnesium bromide gave 87% bis(3,4-methylenedioxyphenyl)methanol. This alc. was α-dehydroxylated by hydrogenation over Pd(OH)2/C (44%), and the resultant bis(methylenedioxy) compound I was deprotected with BBr3 in CH2Cl2 to give 48% invention compound II. In a test for disruption of Alzheimer's Aβ 1-42 fibrils in vitro, the fibrils were incubated for 3 days at 37° in the presence of invention compds., with all compds. giving some degree of dose-dependent disruption. As measured by thioflavin T fluorometry, II gave 57.8% disruption at an Aβ/II weight ratio of 10/1, and its ethylene homolog III gave 69.4% disruption at an Aβ/III weight ratio of 100:1, whereas EDTA gave no significant disruption at any concentration tested. In further bioassays, the invention compds. were similarly potent, dose-dependent disrupters of type 2 diabetes IAPP fibrils, as well as of Parkinson's disease NAC fibrils.

MSTR 1



G1 = 74 / 18-4 20-10 / 23-4 27-10 / 28-4 34-10 / 36-4 37-10 / 39-4 42-10 / 43-4 45-10 / 47-4 52-10 / 54-4 58-10



G2 = carbon chain <containing 1-9 C, up to 2 double bonds, no triple bonds> (opt. substd. by (up to 2) OH)
G3 = NH / O
G11 = carbon chain <containing 1-9 C, up to 2 double bonds, no triple bonds> (opt. substd. by (up to 2) OH)

Patent location: claim 1
Note: and pharmaceutically acceptable salts and esters
Note: substitution is restricted

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:364944 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of diketohydrazine derivatives as cysteine protease inhibitors
INVENTOR(S): Hatayama, Akira; Tsuruta, Hiroshi; Ochi, Yasuo; Imawaka, Haruo
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 231 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091202	A1	20031106	WO 2003-JP5252	20030424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2483998	AA	20031106	CA 2003-2483998	20030424
AU 2003235118	A1	20031110	AU 2003-235118	20030424
EP 1498411	A1	20050119	EP 2003-723188	20030424

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003009670	A	20050315	BR 2003-9670	20030424
CN 1649831	A	20050803	CN 2003-809191	20030424
NZ 536728	A	20060728	NZ 2003-536728	20030424
JP 3812678	B2	20060823	JP 2004-501947	20030424
ZA 2004009502	A	20050815	ZA 2004-9502	20041124
NO 2004005137	A	20041125	NO 2004-5137	20041125
US 2006111303	A1	20060525	US 2006-512348	20060110
JP 2006199703	A2	20060803	JP 2006-46815	20060223
PRIORITY APPLN. INFO.:			JP 2002-123796	20020425
			JP 2004-501947	20030424
			WO 2003-JP5252	20030424

AB Diketohydrazine (3-amino-2-oxopropanoylhydrazine or 3-aminopropionohydrazide) derivs. represented by the following general formula R-AA1-AA2-NR9CR7R8COCONR10NRYRX [wherein R = H, CycA, halo, (un)substituted C1-8 alkyl, R16CO, R16C(S), R16O2C, R16R17NCO, R16SO2, R16COCH2, R16C(S)CH2; CycA = C3-15 mono-, bi-, or tricyclic carbocyclic ring, 3- to 15-membered mono-, bi-, or tricyclic heterocyclic ring containing 1-4 N, 1 or 2 O and/or 1 or 2 S atom(s); R16 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, CycA; R17, R9 = H, C1-4 alkyl, CycA, CycA-C1-4 alkyl; AA1 = a single bond, (un)substituted NR3CR1R2CO, etc.; R1, R2 = H, (un)substituted C1-8 alkyl, CysA, etc.; R3, R7, R8 = H, C1-8 alkyl, CycA, CycA-C1-8 alkyl, etc.; AA2 = a single bond, NR3CR1R2CO, -CycC-CO-, -NR38-CycD-CO-, etc.; CycC = 3- to 17-membered mono or bicyclic heterocyclic ring; CycD = C3-14 mono or bicyclic carbocyclic ring, 3- to 14-membered mono- or bicyclic heterocyclic ring; R38 = group listed in R17; R10, RY, and RX are not defined] and pharmaceutically acceptable salts thereof are prepared These compds. are inhibitors of cysteine protease, in particular cathepsin K, S, L, B, H, F, Y, or C, calpain, or caspase 1. Because of having a cysteine protease inhibitory activity, they are useful as remedies for inflammatory diseases, immune diseases, ischemic diseases, respiratory diseases, circulatory diseases, blood diseases, nerve diseases, liver/biliary duct diseases, bone/joint diseases, metabolic diseases, or diseases caused by apoptosis or degradation of bioconstituent proteins. The bone/joint diseases include osteoporosis, chronic articular rheumatism, arthritis, osteoarthritis (arthrosis deformans), hypercalcemia, bone metastasis of carcinoma, or bone fracture. Also disclosed is a bone absorption inhibitor containing the above compound Because of having an elastase inhibitory activity, these compds. are also useful as remedies for COPD (chronic obstructive pulmonary disease) and so on. N'-(3-tert-butyl-1,3-thiazolidin-2-ylidene)-3-cyclohexylcarbonylamino-2-oxo-3-(tetrahydropyran-4-yl)propionohydrazide hydrochloride inhibited cathepsin K with Ki of 2.5 nM. A tablet and an ampule containing N'-(3-methyl-1,3-thiazolidin-2-ylidene)-(3S)-3-cyclohexylcarbonylamino-2-oxo-5-methylhexanohydrazide hydrochloride were described.

MSTR 1

G24—G26
6

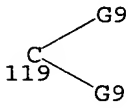
G1 = 155

C(O)-G39
155

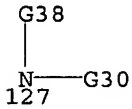
G9 = alkyl <containing 1-8 C> (opt. substd.)
G24 = 5

G1—G72
4 5

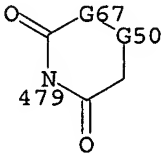
G25 = 119



G26 = 127



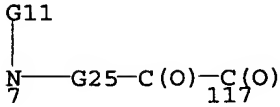
G30 = 479



G39 = 420

O—G63
420

G50 = (0-1) CH2
G63 = cyclopentyl
G67 = CH2
G72 = 7-4 117-6



Patent location: claim 1
Note: or pharmacologically acceptable salts
Note: additional ring formation also claimed

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

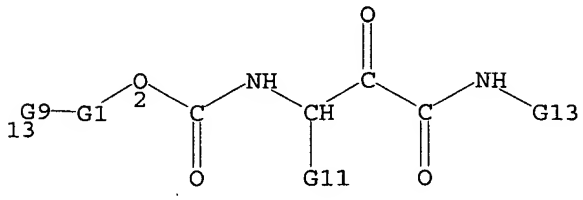
L43 ANSWER 8 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:133839 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of cycloalkyl α-ketoamide derivatives as cathepsin K inhibitors
INVENTOR(S): Catalano, John George; Deaton, David Norman; Miller, Aaron Bayne; Tavares, Francis Xavier
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062192	A1	20030731	WO 2003-US1271	20030115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1465862	A1	20041013	EP 2003-703836	20030115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005515254	T2	20050526	JP 2003-562076	20030115
US 2005054819	A1	20050310	US 2004-501636	20040715
PRIORITY APPLN. INFO.:			US 2002-349812P	20020117
			WO 2003-US1271	20030115

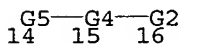
AB Cycloalkyl ketoamide derivs. A-O2CNHCH(D)COCONH-Z [A is the group Q3-Q2-Q1-(CH2)0-2, where Q1 is cycloalkylene, Q2 is null, alkylene (R), OR, SR, NRR' (R' = H, alkyl); Q3 is (un)substituted (hetero)aryl; D is alkyl or amino group-substituted alkyl; Z is the group -X0-2-X10-1-X2, where X is (alkyl)methylene, X1 is CO2CH2, and X2 is (hetero)aryl or

heterocyclyl] were prepared for use as cathepsin K inhibitors in the treatment of disorders, including osteoporosis, associated with enhanced bone turnover which can ultimately lead to fracture. Thus, [1-(4-fluorobenzyl)cyclobutyl]methyl (1S)-1-[oxo(1H-pyrazol-5-ylamino)acetyl]pentylcarbamate was prepared by phosgenation of [1-(4-fluorobenzyl)cyclobutyl]methanol, coupling with Me (2S)-2-aminohexanoate, treatment of the ester with (triphenylphosphoranylidene)acetonitrile, and reaction with 3-aminopyrazole. The product showed Ki < 1 nM for inhibition of cathepsin K.

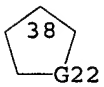
MSTR 1



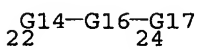
G1 = 16-2 14-13



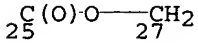
G2 = bond
G4 = 38



G11 = alkyl <containing 1-6 C> (opt. substd. by G12)
G13 = 22



G14 = bond
G16 = 25-22 27-24



G22 = (0-2) CH2
Patent location: claim 1
Note: or salts, solvates, physiologically functional

derivatives

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 9 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 138:215307 MARPAT <<LOGINID::20061206>>
TITLE: Drugs containing chymase inhibitor and ACE inhibitor as the active ingredients
INVENTOR(S): Urata, Hidenori; Hase, Naoki; Tsuchiya, Naoki
PATENT ASSIGNEE(S): Teijin Limited, Japan
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018061	A1	20030306	WO 2002-JP8572	20020826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442761	AA	20030306	CA 2002-2442761	20020826
EP 1419785	A1	20040519	EP 2002-760743	20020826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1520314	A	20040811	CN 2002-812646	20020826
US 2004122042	A1	20040624	US 2003-474334	20031008
PRIORITY APPLN. INFO.:			JP 2001-254120	20010824
			WO 2002-JP8572	20020826

AB It is intended to provide drugs efficacious in treating hypertension, heart diseases (megalocardia, heart failure, myocardial infarction, etc.), cerebral attack, nephritis and the like. Namely, remedies for circulatory diseases wherein a chymase inhibitor and an ACE inhibitor can be used together; and a method of treating circulatory diseases associated with the simultaneous occurrence of chymase inhibition and ACE inhibition.

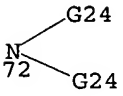
MSTR 3

G10—G35
88

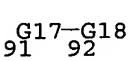
G7 = Ph (opt. substd.)
G10 = 128

HN——G16
128

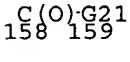
G14 = 72



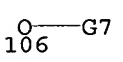
G16 = 91



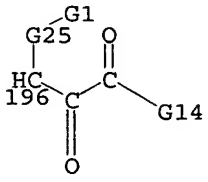
G17 = 158-128 159-92



G18 = 106



G21 = (0-3) CH2
G24 = Ph (opt. substd.)
G25 = alkylene (opt. substd. by 1 or more G26)
G35 = 196



Derivative: or pharmacologically acceptable salts
Patent location: claim 12

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

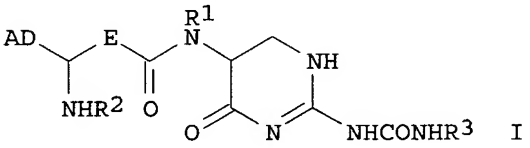
L43 ANSWER 10 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:47208 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of ureidodihydropyrimidinones as antibacterials.
INVENTOR(S): Raddatz, Siegfried; Brands, Michael; Endermann, Rainer; Gahlmann, Reinhold; Geschke, Frank-Ulrich; Kroll, Hein-Peter; Krueger, Joachim; Stoltefuss, Juergen
PATENT ASSIGNEE(S): Bayer AG, Germany

SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10061538	A1	20020620	DE 2000-10061538	20001211

PRIORITY APPLN. INFO.: DE 2000-10061538 20001211

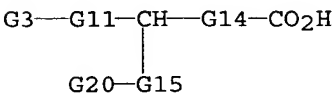
GI



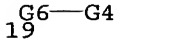
I

AB Title compds. [I; R1, R2, R8 = H, alkyl; A = R4R5N, R6R7NC(:Q)NR5, R8C(:NR9)NR5; R4-R7, R9 = H, alkyl, alkanoyl, PhCH2, pyridylmethyl; Q = O, S, NR9; D = (substituted) alkylene; E = bond, CH2; R3 = (substituted) aryl, aroylalkyl, alkoxycarbonyl], were prepared Thus, 5-methylamino-3,4,5,6-tetrahydro-2-(γ-methylureido)pyrimidin-4-one (preparation given), (S)-3,7-dibenzyloxycarbonylaminoheptanoic acid, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU), and diisopropylethylamine were stirred overnight in DMF to give 67.6% protected amide. This was hydrogenated in MeOH over Pd/C to give 52.6% (3'S,5RS)-5-(N-3',7'-diaminoheptanoyl-N-methylamino)-3,4,5,6-tetrahydro-2-(γ-methylureido)pyrimidin-4-one. The latter showed a min. inhibitory concentration of 1.6 μg/mL against S. aureus 133.

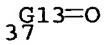
MSTR 3



G3 = 19



G4 = CO2Bu-t
G6 = NH
G11 = 37

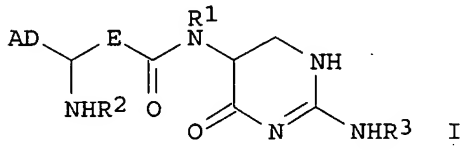


G12 = OH
G13 = carbon chain <containing 2-6 C, saturated>
(opt. substd. by (1-2) G12)
G14 = bond
G15 = NH
G20 = CO2CH2Ph
Patent location: claim 9

L43 ANSWER 11 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:33314 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of arylaminodihydropyrimidinones as antibacterials.
INVENTOR(S): Raddatz, Siegfried; Brands, Michael; Endermann, Rainer; Gahlmann, Reinhold; Geschke, Frank-Ulrich; Kroll, Hein-Peter; Krueger, Joachim; Stoltefuss, Juergen
PATENT ASSIGNEE(S): Bayer AG, Germany
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10061541	A1	20020620	DE 2000-10061541	20001211

PRIORITY APPLN. INFO.: DE 2000-10061541 20001211
GI



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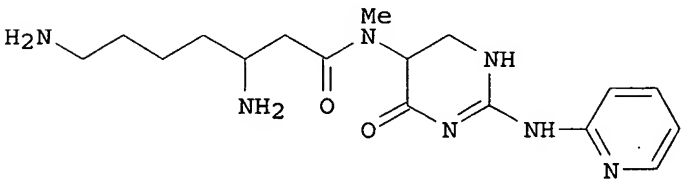
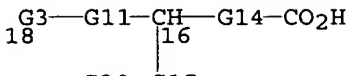


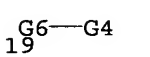
II

AB Title compds. [I; A = R4R5N, R6R7NC(:Q)NR5, R6C(:NR9)NR5; R4-R7, R9 = H, alkyl, alkanoyl, PhCH2, pyridylmethyl; R8 = H, alkyl; Q = O, S, NR9; D = (substituted) alkylene; E = bond, CH2; R2 = H, alkyl; R3 = (substituted) aryl, (unsatd.) heterocyclyl], were prepared Thus, title compound (II) (general preparation given) showed a min. inhibitory concentration of 0.06 against S.
aureus 133.

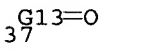
MSTR 3



G3 = 19



G4 = CO2Bu-t
G6 = NH
G11 = 37



G12 = OH
G13 = carbon chain <containing 2-6 C, saturated>
(opt. substd. by (1-2) G12)
G14 = bond
G15 = NH
G20 = CO2CH2Ph
Patent location: claim 9

L43 ANSWER 12 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:263157 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of indazoles having an action similar to that of a thyroid hormone, method for the production thereof, and their use in medicaments
INVENTOR(S): Woltering, Michael; Haning, Helmut; Schmidt, Gunter; Pernerstorfer, Josef; Bischoff, Hilmar; Kretschmer, Axel; Voehringer, Verena; Faeste, Christiane
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

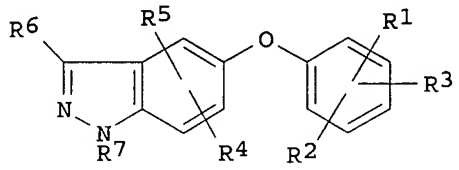
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022586	A1	20020321	WO 2001-EP10204	20010905

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

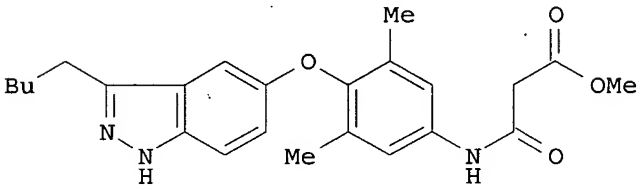
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10046029	A1	20020328	DE 2000-10046029	20000918
AU 2002010484	A5	20020326	AU 2002-10484	20010905
CA 2422353	AA	20030314	CA 2001-2422353	20010905
EP 1324987	A1	20030709	EP 2001-978337	20010905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002193610	A1	20021219	US 2001-956566	20010918
US 6608049	B2	20030819		
PRIORITY APPLN. INFO.:			DE 2000-10046029	20000918
			WO 2001-EP10204	20010905

GI



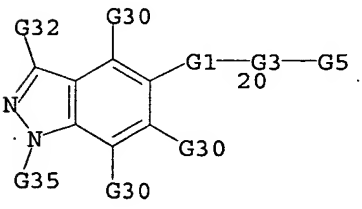
I



II

AB Title compds. [I; Z = O, S, CH2, CHF, CF2; R1, R2 independently = H, halo, C1-6 alkyl, CF3, CHF2, CH2F, CH2:CH, C3-7 cycloalkyl; R3 = A(CH2)n(CO)mR8; A = O, S, CH2, CO, NR9; n = 0, 1, 2, 3; m = 0, 1, 2; R8 = C1-8 alkyl, C6-10 aryl; C3-8 cycloalkyl, OR10, NR11R12; R9 = H, C1-6 alkyl, C3-8 cycloalkyl; R10, R11, R12 independently = H, OH, OC6H5, OCH2C6H5; R4, R5 independently = OH, halo, CN, NO2, C1-4 alkyl; R6 = alkyl; R7 = H, COR; R = COOCH2CH3, OC(CH3)3] and salts are prepared and may be used for prophylaxis or treatment of arteriosclerosis and hypercholesterolemia. Title compds. I have an action similar to that of a thyroid hormone. The invention also relates to a method for producing said indazole derivs., and to their use in medicaments. Thus, the title compound II was prepared and in vitro tested for T3 promoter assay.

MSTR 1



G3 = phenylene (opt. substd. by (up to 2) G4)
G5 = 63

G26—G24
63 64

G17 = Ph (opt. substd.)
G19 = 47

O——G17
47

G20 = 53

N——G7
53

G24 = alkyl <containing 1 or more C>
(opt. substd. by (1-3) G25)
G25 = 90

HN——C(O)-G19
90

G26 = 73-20 72-64

G20—C(O)-C(O)
73 72

G32 = 128

G33—G24
128

Patent location: claim 1
Note: substitution is restricted

MSTR 3

G1——G3——G5
20

G3 = phenylene (opt. substd. by (up to 2) G4)
G5 = 63

G26—G24
63 64

G17 = Ph (opt. substd.)
G19 = 47

O——G17
47

G20 = 53

N——G7
53

G24 = alkyl <containing 1 or more C>
(opt. substd. by (1-3) G25)
G25 = 90

HN——C(O)-G19
90

G26 = 73-20 72-64

G20—C(O)-C(O)
73 72

Patent location: claim 4
Note: substitution is restricted

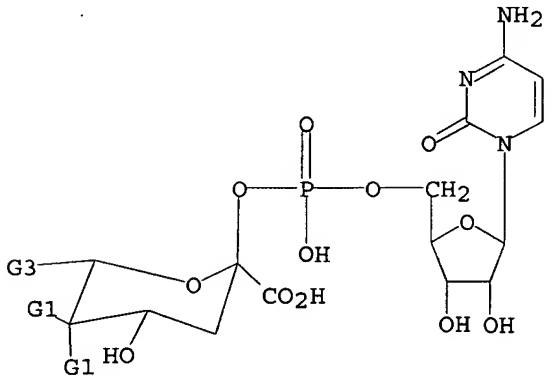
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 13 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 131:271018 MARPAT <<LOGINID::20061206>>
TITLE: Production of CMP-sialate synthase with recombinant prokaryotes and use of enzyme for synthesis of CMP-sialic acid analogs and derivatives
INVENTOR(S): Fessner, Wolf-Dieter; Knorst, Marion
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19913206	A1	19991007	DE 1999-19913206	19990324
PRIORITY APPLN. INFO.:			DE 1999-19913206	19990324
			DE 1998-19813426	19980326

AB The title method for preparing Neisseria meningitidis CMP-sialate synthase and its use in preparing CMP-sialic acid analogs and oligosaccharides and glycoconjugates containing the sialic acid analogs are disclosed. Thus, the enzyme was produced with siaB gene-expressing Escherichia coli and was used to prepare CMP-sialic acid analogs and disaccharides containing these analogs.

MSTR 1



G2 = CH2Ph
G3 = 60

G7═O
60

G6 = OH / 66

HN──C(O)-O──G2
66

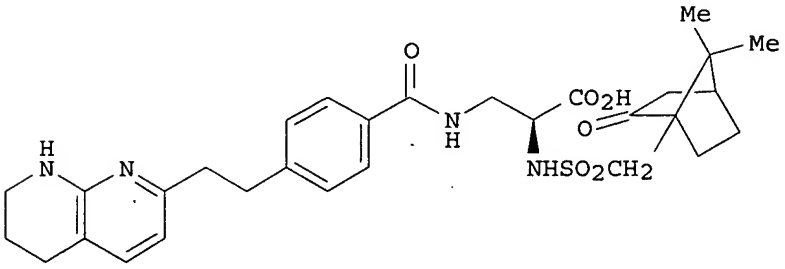
G7 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G6)
Patent location: claim 11

L43 ANSWER 14 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 129:136499 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of heterocyclic peptide derivatives as integrin antagonists
INVENTOR(S): Duggan, Mark E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831359	A1	19980723	WO 1998-US617	19980113
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2277273	AA	19980723	CA 1998-2277273	19980113
AU 9860231	A1	19980807	AU 1998-60231	19980113
AU 729869	B2	20010215		
US 6017925	A	20000125	US 1998-6626	19980113
EP 1007026	A1	20000614	EP 1998-903466	19980113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001509176	T2	20010710	JP 1998-534473	19980113
PRIORITY APPLN. INFO.:			US 1997-35614P	19970117
			GB 1997-2788	19970211
			US 1997-62594P	19971020
			GB 1997-25996	19971209
			WO 1998-US617	19980113

GI

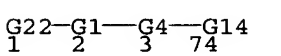


I

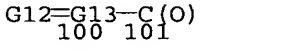
AB Novel compds. X-Y-Z-Aryl-A-B [Aryl = 5-6 membered aromatic ring containing 0-3 N atoms and substituted with R8 and R9; X = NR1R2, NR1CR3:NR2, C(NR2R3):NR1, NR1C(NR3R4):NR2; aryl-NR1R2, aryl-C(NR2R3):NR1, aryl-NR1C(NR3R4):NR2, 5- to 6-membered (non)aromatic ring containing 0-4 N, O, or S atoms and substituted with R1-R4, 9-14 membered polycyclic ring containing 0-4 N, O, or S atoms and substituted with R1-R4; Y = C0-8 alkylene, C3-10 cycloalkyl, C0-8 alkylene-Y1-C0-8 alkylene, (CH2)0-6-aryl-Y2-(CH2)0-6 alkylene; Y1 = NR10CO, CONR10, O, NR10, S(O)0-2, SO2NR10, NR10SO2, CO, CH(OR1); Y2 = bond, CO, CONR10, NR10CO; Z, A = independently (CH2)m, (CH2)m-Z1-(CH2)n; Z1 = O, NR11, NR11CONR12, CONR11, NR11CO, CO, C(S), S(O)0-2, SO2NR11, NR11SO2, CR11:CR12, C.tplbond.C; m, n = 0-6; B = (CR6R7)pCOR13; p = 1-3;

R1-R5, R8-R12 = independently H, halo, C1-10 alkyl, aryl-C0-8 alkyl, amino-C0-8 alkyl, C1-3 acylamino-C0-8 alkyl, C1-6 alkylamino-C0-8 alkyl, C1-6 dialkylamino-C0-8 alkyl, aryl-C0-6 alkylamino-C0-6 alkyl, C1-4 alkoxyamino-C0-6 alkyl, etc; R6 = H, F, C1-8 alkyl, OH, C1-6 alkoxy, etc; R7 = (un)substituted C7-20 polycyclyl-C0-8 alkyl-Q-amino-C0-6 alkyl; Q = SO2, CO, NHSO2, NHCO, O2C; R13 = OH, C1-8 alkoxy, C1-8 alkylcarbonyloxy-C1-4 alkoxy, L- or D-amino acid residue, etc.] and derivs. are described as vitronectin antagonists. The vitronectin receptor antagonist compds. of the present invention are αvβ3 antagonists, αvβ5 antagonists or dual αvβ3/αvβ5 antagonists useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammation, viral disease, and tumor growth. Thus, peptide analog I was prepared in several steps from protected (S)-2,3-diaminopropanoic acid, (-)-10-camphorsulfonyl chloride, and 4-[2-(1,2,3,4-tetrahydro-1,8-naphthyridin-7-yl)ethyl]benzoic acid (preparation given). Test procedures to measure αvβ3 binding and bone resorption inhibiting activity are described.

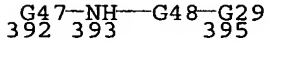
MSTR 1



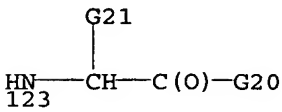
G4 = 100-2 101-74



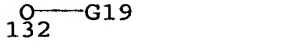
G11 = 1 or more 392



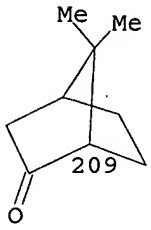
G12 = O
G13 = carbon chain <containing 2 or more C>
(substd. by 1 or more G11)
G14 = 123



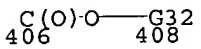
G19 = carbon chain <containing 1-6 C>
G20 = 132



G29 = 209



G32 = bond
G47 = bond
G48 = 406-393 408-395



Derivative: and pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 15 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 128:128280 MARPAT <<LOGINID::20061206>>
TITLE: Carbonylation process and catalysts for the preparation of N-acylglycine derivatives from carboxamides and aldehydes
INVENTOR(S): Geissler, Holger; Bogdanovic, Sandra
PATENT ASSIGNEE(S): Hoechst Research and Technology Deutschland GmbH and Co. KG, Germany; Geissler, Holger; Bogdanovic, Sandra
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

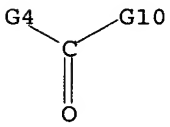
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804518	A1	19980205	WO 1997-EP3853	19970718
W: AU, BR, BY, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, RU, SG, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19629717	C1	19980212	DE 1996-19629717	19960725
CA 2261853	AA	19980205	CA 1997-2261853	19970718
AU 9737680	A1	19980220	AU 1997-37680	19970718
EP 918745	A1	19990602	EP 1997-934485	19970718
EP 918745	B1	20011128		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
CN 1228078	A	19990908	CN 1997-196676	19970718
HU 9903312	A2	20000228	HU 1999-3312	19970718

JP 2001505871	T2	20010508	JP 1998-508444	19970718
ZA 9706596	A	19990125	ZA 1997-6596	19970724
NO 9900295	A	19990122	NO 1999-295	19990122
US 2001007911	A1	20010712	US 1999-230203	19990707
US 2003078436	A1	20030424	US 2002-280866	20021025
PRIORITY APPLN. INFO.:			DE 1996-19629717	19960725
			WO 1997-EP3853	19970718
			US 1999-230203	19990707

OTHER SOURCE(S): CASREACT 128:128280

AB N-acylglycine derivs. R1CONR2CH(R)CO2H [R = H, CO2H, (un)saturated (un)branched alkyl, alkenyl, aryl, etc.; R1 = H, (un)branched alkyl, cycloalkyl, alkenyl, aryl, etc.; R2 = H, (un)branched alkyl, cycloalkyl, alkenyl, aryl, etc.] (e.g., N-acetylleucine) are prepared in high yield and selectivity by the CO carbonylation of a carboxamide R1CONH(R2) and an aldehyde RCHO in the presence of a solvent and a catalyst system comprising a palladium compound (e.g., PdBr2), an ionic halide (e.g., LiBr), and an acid (e.g., H2SO4) at 20-200°/1-150 bars.

MSTR 1



G1 = 8

G2═O
8

G2 = carbon chain <containing 1-10 C>
(opt. substd. by 1 or more G9)
G4 = aryl <containing 6-18 C>
(opt. substd. by 1 or more G7) /
aryl <containing 6-18 C> (substd. by 1 or more G8)
G7 = 21 / 25

HN—C(O)-O—Bu-t (21) HN—C(O)-O—CH_2—Ph (25)

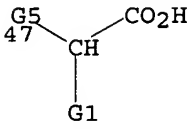
G8 = 21 / 25

HN—C(O)-O—Bu-t (21) HN—C(O)-O—CH_2—Ph (25)

G9 = OH / 21 / 25

HN—C(O)-O—Bu-t (21) HN—C(O)-O—CH_2—Ph (25)

G10 = 47



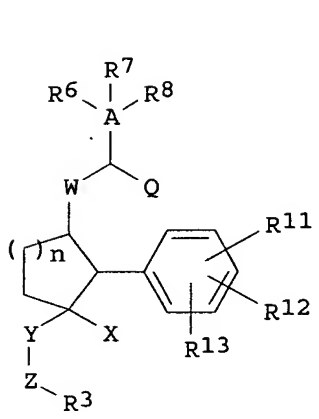
Patent location: claim 1

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

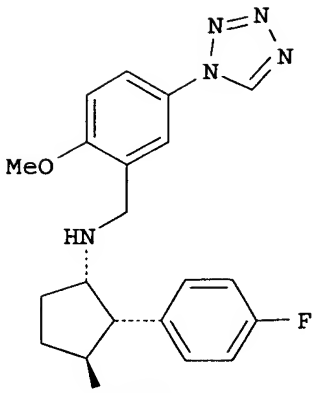
L43 ANSWER 16 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 127:17433 MARPAT <<LOGINID::20061206>>
TITLE: Cyclopentyl tachykinin receptor antagonists
INVENTOR(S): Finke, Paul E.; Maccoss, Malcom; Meurer, Laura C.; Mills, Sander G.; Caldwell, Charles G.; Chen, Ping; Durette, Philippe L.; Hale, Jeffery; Holson, Edward; Kopka, Ihor; Robichaud, Albert
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Finke, Paul E.; Maccoss, Malcolm; Meurer, Laura C.; Mills, Sander G.; Caldwell, Charles G.; Chen, Ping; Durette, Philippe L.; Hale, Jeffrey; et al.
SOURCE: PCT Int. Appl., 343 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714671	A1	19970424	WO 1996-US16489	19961015
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2234913	AA	19970424	CA 1996-2234913	19961015
AU 9710497	A1	19970507	AU 1997-10497	19961015
AU 722883	B2	20000810		
EP 858444	A1	19980819	EP 1996-941315	19961015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002534955	T2	20021015	JP 1997-515929	19961015
PRIORITY APPLN. INFO.:			US 1995-5558P	19951018
			GB 1996-5160	19960312
			WO 1996-US16489	19961015

GI



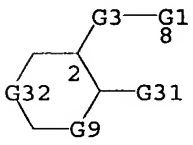
I



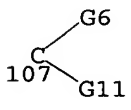
II

AB The invention is directed to certain novel compds. I and their pharmaceutically acceptable salts [wherein R3 = H, OH, alkoxy, Ph, cyano, halo, (un)substituted NH2, heterocyclyl, etc.; R6, R7, R8 = H, alkoxy, halo, (un)substituted alkyl, OH, cyano, CF3, etc.; R11, R12, R13 = H, (un)substituted alkyl, halo, cyano, CF3, etc.; A = benzene or various heterocycles; Q = H, alkyl; W = O, NH, alkylimino, NHCO, alkyliminocarbonyl; X = H, alkyl; Y = bond, (un)substituted alkyl; Z = (un)substituted NH, CONH, NHCO, SO2NH, NHSO2, SO2, CO2H, etc.; n = 1, 2, 3]. The invention is also concerned with pharmaceutical formulations comprising I as active ingredients, and use of I and their formulations in the treatment of certain disorders. I are tachykinin receptor antagonists (no data) and are useful in the treatment of inflammatory diseases, pain, migraine, asthma, and emesis. For instance, reductive alkylation of the appropriate amine with 2-methoxy-5-(1-tetrazolyl)benzaldehyde, by treatment with AcOH and 3A sieves in MeOH followed by NaBH3CN, gave title compound II.

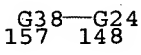
MSTR 1



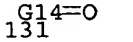
G9 = 107



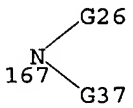
G11 = 157



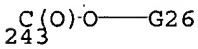
G14 = carbon chain <containing 1-6 C, saturated>
(opt. substd.)
G17 = 131



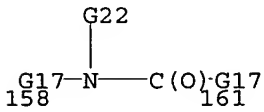
G24 = 167



G26 = Ph
G32 = (0-2) CH2
G37 = 243



G38 = 158-107 161-148



Derivative: or pharmaceutically acceptable salts
Patent location: claim 1
Note: additional substitution also claimed
Note: substitution is restricted

L43 ANSWER 17 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 126:103152 MARPAT <<LOGINID::20061206>>
TITLE: Production of peptides and N-carbamoyl-protected peptides
INVENTOR(S): Bommarius, Andreas; Drauz, Karlheinz; Eichhorn, Uwe; Jakubke, Hans-Dieter; Kottenhahn, Matthias
PATENT ASSIGNEE(S): Degussa AG, Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

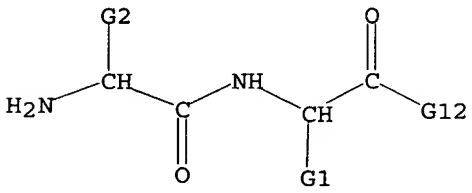
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19607100	A1	19970116	DE 1996-19607100	19960226
DE 19607100	C2	20000427		
CA 2227732	AA	19970130	CA 1996-2227732	19960626
WO 9703091	A1	19970130	WO 1996-EP2782	19960626
W: AU, BR, CA, CN, CZ, HU, IS, JP, KR, MX, NO, NZ, RU, SG, SI, SK, TR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9664165	A1	19970210	AU 1996-64165	19960626
EP 839153	A1	19980506	EP 1996-923933	19960626
EP 839153	B1	20010816		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, IE, FI				
CN 1190406	A	19980812	CN 1996-195353	19960626
JP 11508452	T2	19990727	JP 1996-505455	19960626
AT 204291	E	20010915	AT 1996-923933	19960626
ES 2160827	T3	20011116	ES 1996-923933	19960626
EP 1170301	A1	20020109	EP 2001-102668	19960626
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, IE, FI				
ZA 9605813	A	19970127	ZA 1996-5813	19960709
US 6251625	B1	20010626	US 1998-11859	19980403
PRIORITY APPLN. INFO.:			DE 1995-19524710	19950711
			DE 1996-19603844	19960205
			DE 1996-19607100	19960226
			EP 1996-923933	19960626
			WO 1996-EP2782	19960626

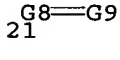
OTHER SOURCE(S): CASREACT 126:103152

AB A procedure for the enzymic production of di- and oligopeptides and the splitting of the protecting group used are claimed. The procedure comprises a simple and inexpensive peptide synthesis and a useful cleavage procedure. It involves 3 steps: (1) preparation of N-carbamoylamino acids or N-carbamoylamino acid derivs., (2) enzymic formation of the peptide bond between a carbamoyl-protected electrophile and a nucleophile, and (3) chemical or enzymic removal of the carbamoyl protecting group.

MSTR 1



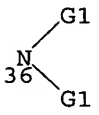
G1 = 21



G2 = OH / 12

G3—G4
12

G3 = NH / O
G4 = CH2Ph
G8 = carbon chain <containing 1-6 C, saturated>
(opt. substd. by G2)
G9 = O
G12 = 36

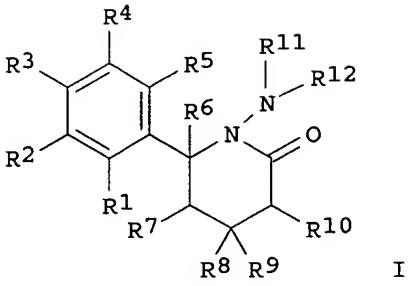


Patent location: claim 1
Note: additional interruptions of alkyl in G1 also claimed

L43 ANSWER 18 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 126:74748 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of 1-(N-amino)-2-phenyl-6-piperidone herbicides
INVENTOR(S): Hill, Regina Luise; Von Deyn, Wolfgang; Kardorff, Uwe; Engel, Stefan; Otten, Martina; Vossen, Marcus; Klintz, Ralf; Walter, Helmut; Mislitz, Ulf; Westphalen, Karl-Otto
PATENT ASSIGNEE(S): BASF A.-G., Germany
SOURCE: Ger. Offen., 75 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19518739	A1	19961128	DE 1995-19518739	19950522
CA 2218550	AA	19961128	CA 1996-2218550	19960508
WO 9637471	A1	19961128	WO 1996-EP1923	19960508
W: AU, BG, BR, CA, CN, CZ, EE, GE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, SG, SK, TR, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9658156	A1	19961211	AU 1996-58156	19960508
EP 815083	A1	19980107	EP 1996-919712	19960508
R: CH, DE, FR, GB, LI				
JP 11511743	T2	19991012	JP 1996-535302	19960508
ZA 9604034	A	19971121	ZA 1996-4034	19960521
US 6028033	A	20000222	US 1997-952251	19971106
PRIORITY APPLN. INFO.:			DE 1995-19518739	19950522
			WO 1996-EP1923	19960508

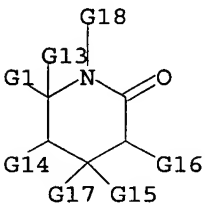
GI



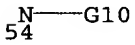
I

AB The title compds. [I; R1-R5 = H, OH, CN, halogen, OCN, SCN, SF5, (un)substituted NH2, alkyl, etc.; R6, R7 = H, a single bond; R8 = H, cycloalkyl, (un)substituted alkyl, etc.; R9, R10 = H, single bond; R11 = H, (un)substituted alkyl, alkenyl, alkynyl, etc.; R12 = H, alkyl, cycloalkyl; etc.] (e.g., II; m.p. 106-109°), useful as agrochem. herbicides, are prepared and I-containing formulations presented.

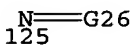
MSTR 1



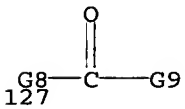
G8 = NH / 54



G9 = alkoxy <containing 1-4 C> (opt. substd.) / OPh (opt. substd.)
G18 = 125

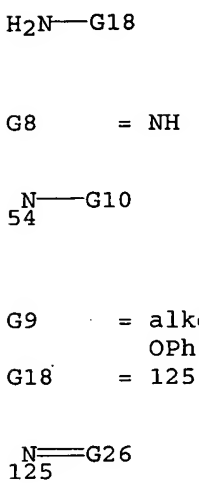


G26 = carbon chain <0 or more double bonds, 0 or more triple bonds> (opt. substd. by (1-2) G27)
G27 = OH / 127



Patent location: claim 1

MSTR 6



Patent location: claim 3

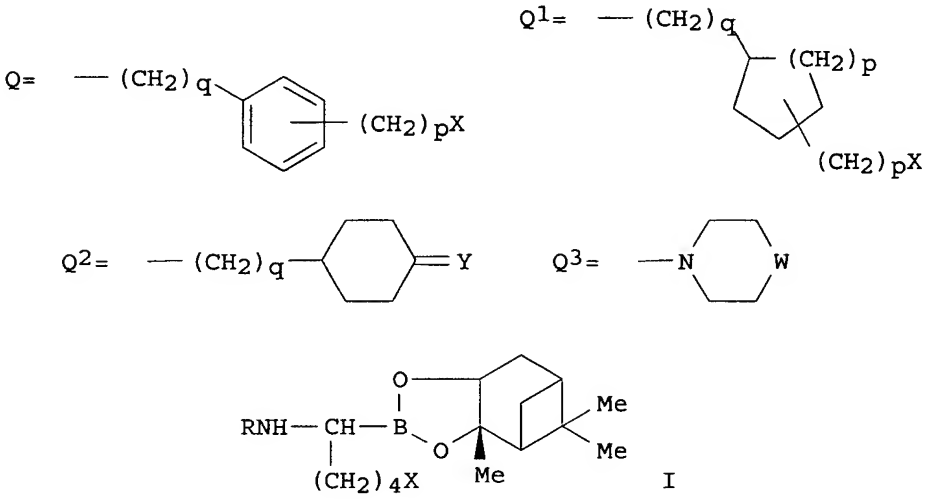
L43 ANSWER 19 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 125:143313 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of amidino and guanidino substituted peptide analogs as inhibitors of trypsin-like enzymes
INVENTOR(S): Lee, Sheng-lian O.; Carini, David John; Fevig, John Matthew; Kettner, Charles Adrian; Mantri, Padmaja; Feng, Zixia
PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Company, USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612499	A1	19960502	WO 1995-US13702	19951024

W: AU, CA, JP, MX, NZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5658885	A	19970819	US 1994-329039	19941025
AU 9539671	A1	19960515	AU 1995-39671	19951024
EP 787010	A1	19970806	EP 1995-937612	19951024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10508010	T2	19980804	JP 1995-514116	19951024
PRIORITY APPLN. INFO.:			US 1994-329039	19941025
			US 1993-52835	19930427
			US 1994-204055	19940302
			WO 1995-US13702	19951024

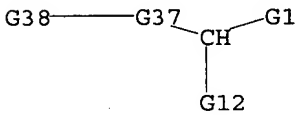
GI



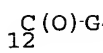
AB Novel α-amino acid and α-aminoboronic acid and corresponding peptide analogs of formula R3[A]nNR2CHR1E [E = BY1Y2, COR14, CO2R4, CONR15R16, COR4, COCO2R4; wherein Y1, Y2 = OH, F, (un)substituted NH2; or Y1Y2 = cyclic boron ester, cyclic boron amide, or cyclic boron amide-ester containing 2-20 carbon atoms and optionally 1-3 heteroatoms selected from N, S, and O; R4 = H, C1-4 alkyl, aryl-C1-4 alkyl, C5-7 cycloalkyl; R14 = CF3, CHF2, CH2F, CH2Cl, CO2R4, CONR15R16, COR4, etc.; R15, R16 = H, C1-4 alkyl, aryl-C1-4 alkyl, C5-7 cycloalkyl, (un)substituted Ph; or NR15R16 = Q3; wherein W = single bond, O, S, SO, SO2, CH2, NR4, NCOR4; R1 = (un)substituted C1-12 alkyl, Q, Q1; wherein X = halo, cyano, NO2, CF3, NH2, NHC(:NH)H, NHC(:NH)NHOH, NHC(:NH)NHCN, etc.; Y = O, :NOH, :NNHCHO; p = 0-3; q = 0-4; R2 = H, (un)substituted C1-12 alkyl, cycloalkyl, Ph, naphthyl, or aryl-C1-4 alkyl; R3 = H, alkyl, aryl, alkylaryl, S(O)rR7, COR7, CO2R7, P(O)2OR7, or any other C1-20 NH2-blocking group; wherein R7 = H, C1-4 alkyl, (un)substituted Ph, naphthyl, or aryl-C1-4 alkyl; r = 0-2; A = amino acid residue or peptide comprised of 2-20 amino acids residue; n = 0,1] and pharmaceutically acceptable salts thereof are prepared These peptide analogs are useful for treating a physiol. disorder in a warm blooded animal catalyzed by trypsin-like enzymes, e.g. blood clotting, arterial thrombosis, myocardial infarction, inflammation, pancreatitis, and hereditary angioedema. Trypsin-like enzymes are a group of proteases which hydrolyze peptide bonds at basic residues liberating either a C-terminal arginyl or lysyl residue, among which are enzymes of the blood

coagulation and fibrinolytic system required for hemostasis (e.g. factors II, X, VII, IX, kallikrein, tissue plasminogen activators, urokinase-like plasminogen activator, and plasmin), enzymes of the complement system, acrosin, and pancreatic trypsin. Thus, Ac-D-Phe-Pro-OH was condensed with a boronic acid derivative (I; R = H, X = Br) by a mixed anhydride procedure using iso-Bu chloroformate and N-methylmorpholine in CCl4 to give an intermediate I (R = Ac-D-Phe-Pro, X = Br), which was heated with Bu4NCN in MeCN at 90° for 3 h to give the nitrile I (R = Ac-D-Phe-Pro, X = cyano). The latter nitrile was stirred with saturated methanolic HCl at 4° overnight, concentrated, and redissolved in MeOH. NH3(g) was bubbled through the solution for 1 h and the solution was heated at 50° for 3 h to give I [R = Ac-D-Phe-Pro, X = C(:NH)NH2]. This compound in vitro inhibited thrombin with Ki of <500 nM.

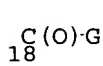
MSTR 1B



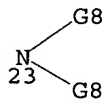
G1 = 12



G4 = 18



G6 = 23



G8 = Ph (opt. substd.)
G12 = 59 / 61

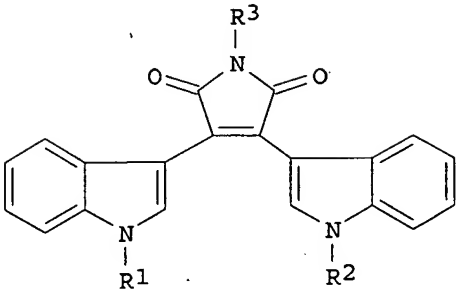
G13 = alkylene <containing 1-12 C>
G37 = NH
G38 = CO2CH2Ph
Derivative: and pharmaceutically acceptable salts

Patent location: claim 1
Note: substitution is restricted
Note: alkyl groups in G18 may contain heteroatom interruptions

L43 ANSWER 20 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 124:343107 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of 3,4-bis(3-indolyl)-1H-pyrrole-2,4-dione derivatives as protein kinase C inhibitors.
INVENTOR(S): Gillig, James R.; Jirousek, Michael R.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 263,912.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5491242	A	19960213	US 1995-404218	19950315
US 5481003	A	19960102	US 1994-263912	19940622
CA 2193703	AA	19951228	CA 1995-2193703	19950619
CA 2193703	C	20060321		
WO 9535294	A1	19951228	WO 1995-US7791	19950619
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9528669	A1	19960115	AU 1995-28669	19950619
EP 766682	A1	19970409	EP 1995-923985	19950619
EP 766682	B1	20010808		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10502910	T2	19980317	JP 1995-502555	19950619
AT 203991	E	20010815	AT 1995-923985	19950619
ES 2159318	T3	20011001	ES 1995-923985	19950619
PT 766682	T	20011130	PT 1995-923985	19950619
GR 3037074	T3	20020131	GR 2001-401946	20011030
PRIORITY APPLN. INFO.:			US 1994-263912	19940622
			US 1995-404218	19950315
			WO 1995-US7791	19950619

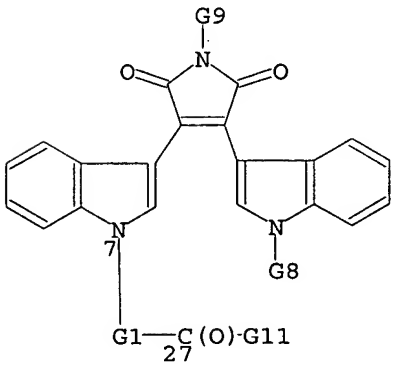
GI



I

AB The invention discloses compds. I [R1 = XCOCHR4NHP1; R2 = acyl, alkoxyalkyl, hydroxyalkyl, dialkylaminoalkyl, azidoalkyl, amino acid group COCHR4NHP1, etc.; R3 = H, Me; R4 = amino acid sidechain; X = (CH2)nNH, (CH2)nO, C6H4NH, C6H4O, bond; P1 = H, alkyl, protecting group; n = 1-3] and their pharmaceutically acceptable salts and solvates. I are highly isoenzyme-selective inhibitors of protein kinase C (PKC) beta-1 and beta-2 isoenzymes, and are therapeutically useful in treating conditions associated with diabetes mellitus and its complications, as well as other disease states associated with an elevation of the beta-1 and beta-2 isoenzyme. For example, N-acylation of 3-[1-(3-azidopropyl)-3-indolyl]-4-[3-indolyl]-1H-pyrrole-2,5-dione by Boc-Gly-OC6H4NO2-p in dry MeCN in the presence of KF, 18-crown-6, and DIPEA, gave invention compound I [R1 = N3(CH2)3; R2 = Boc-Gly-; R3 = H] (II). In an assay against 8 PKC isoenzymes, II had the following IC50 values (μM): α 1.4, β1 0.26, β2 0.031, γ 19, δ 4.6, ε (no data), ζ 100, and η 2.6.

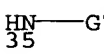
MSTR 1



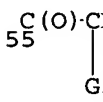
G1 = 28-7 29-27 / 30-7 31-27

G2 = (1-3) CH2
G3 = NH

G5 = Me
G6 = 35



G7 = CO2Ph
G11 = 55

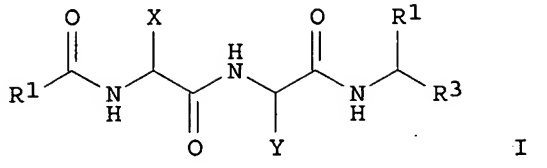


Derivative: or pharmaceutically acceptable salts or solvates
Patent location: claim 1

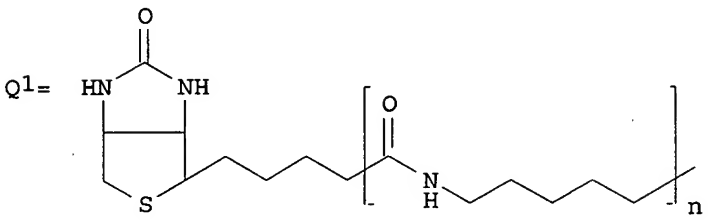
L43 ANSWER 21 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 123:84007 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of peptideamide endothelin converting enzyme inhibitors.
INVENTOR(S): Leban, Johann Jakob; Sherman, Douglas Byron; Sigafoos, James Frederick; Spaltenstein, Andreas; Viveros, Osvaldo Humberto; Wan, David Chi-cheong
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9415956	A1	19940721	WO 1994-GB9	19940104
W: AU, CA, CN, FI, HU, JP, KR, NO, NZ, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9400008	A	19950703	ZA 1994-8	19940103
AU 9458202	A1	19940815	AU 1994-58202	19940104
EP 677059	A1	19951018	EP 1994-903951	19940104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08506569	T2	19960716	JP 1994-515796	19940104
JP 3529381	B2	20040524		
EP 1029869	A1	20000823	EP 2000-201447	19940104
EP 1029869	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 238343	E	20030515	AT 2000-201447	19940104
ES 2193919	T3	20031116	ES 2000-201447	19940104
US 6235717	B1	20010522	US 1995-481365	19950703
PRIORITY APPLN. INFO.:			GB 1993-48	19930104
			EP 1994-903951	19940104
			WO 1994-GB9	19940104

GI

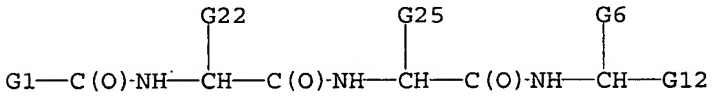


I

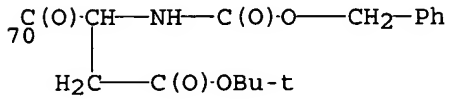


AB Title compds. I; R1 = alkyl, carboxyalkyl, alkoxycarbonylalkyl, (substituted) aryl, aralkyl, aralkoxy, aryloxyalkyl, diphenylalkyl, Q1, R5CONH(CH2)5[Z(CH2)5]n, PhCH2O2CNHCH(CH2CO2R6); n = 0,1; Z = CONH, CH2; R5 = PhCH2O, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl, 2,5-dioxo-4-imidazolidinyl; R6 = H, alkyl; R2 = indol-3-ylmethyl, (substituted) aryl, aralkyl; R3 = CHO, maleimidomethyl, methoxycarbonylvinyl, dimethoxymethyl, semicarbaxonomethyl, alkyl, etc.; X = alkyl, indolylmethyl, naphthylmethyl, benzyloxybenzyl, cycloalkylmethyl, (substituted) PhCH2; Y = indolylmethyl, naphthylmethyl, benzyloxybenzyl, alkyl, (substituted) PhCH2, were prepared Thus, N-[5-[(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)pentanoyl]-L-p-bromophenylalanyl-L-1-naphthylalanyl-L-N-[1-formyl]-2-(1H-indol-3-yl)ethyl]amide (solution phase preparation given) showed IC50 = 0.002
μM in an endothelin converting enzyme assay in porcine aortal prepns.

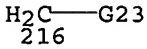
MSTR 1



G1 = 70



G22 = 216



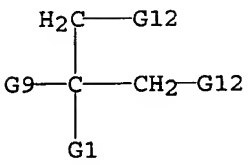
G23 = Ph (opt. substd. by 1 or more G24)
Derivative: or salts
Patent location: claim 1

L43 ANSWER 22 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 122:239193 MARPAT <<LOGINID::20061206>>
TITLE: preparation of 2-amino-1,3-propanediol compounds as immunosuppressants
INVENTOR(S): Fujita, Tetsuro; Sasaki, Shigeo; Yoneta, Masahiko; Mishina, Tadashi; Adachi, Kunitomo; Chiba, Kenji
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan; Taito Co., Ltd.
SOURCE: PCT Int. Appl., 405 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

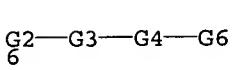
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9408943	A1	19940428	WO 1993-JP1515	19931018
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2126337	AA	19940428	CA 1993-2126337	19931018
CA 2126337	C	20030624		
EP 627406	A1	19941207	EP 1993-923035	19931018
EP 627406	B1	19981028		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 2579602	B2	19970205	JP 1993-509845	19931018
AT 172711	E	19981115	AT 1993-923035	19931018
ES 2126658	T3	19990401	ES 1993-923035	19931018
US 5604229	A	19970218	US 1994-244942	19940617
US 5719176	A	19980217	US 1996-725890	19961002
US 5952316	A	19990914	US 1997-911602	19970814
HK 1013281	A1	20000602	HK 1998-114539	19981222
PRIORITY APPLN. INFO.:			JP 1992-283281	19921021
			JP 1993-179427	19930720
			WO 1993-JP1515	19931018
			US 1994-244942	19940617
			US 1995-478834	19950607

AB R2R3NCR(CH2OR4)CH2OR5 [I; R = (un)substituted linear or branched C chain, aryl, cycloalkyl; R2-R5 = H, alkyl, aralkyl, acyl, alkoxycarbonyl] and their pharmaceutically acceptable salts are prepared Alkylation of di-Et 2-acetamidomalonate with tetradecyl bromide and NaOEt in EtOH gave di-Et 2-acetamido-2-tetradecylmalonate, which was reduced with LiAlH4 in THF and acetylated with Ac2O in pyridine to give diacetate I (R = tetradecyl, R2 = H, R3 = R4 = R5 = Ac). Also prepared were 398 addnl. I, which showed IC50 of 1-50 nM in mouse mixed lymphocyte reaction.

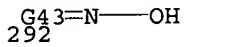
MSTR 1



G1 = 6



G2 = 292



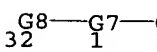
G3 = NH
G7 = alkoxycarbonylamino /
alkylcarbonyloxy <containing 1-20 C> (opt. substd. by Ph) /
OH
G43 = carbon chain <containing 1-29 C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G7)
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

L43 ANSWER 23 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 120:134484 MARPAT <<LOGINID::20061206>>
TITLE: Heterocyclic HIV retroviral protease inhibitors
INVENTOR(S): Dreyer, Geoffrey Bainbridge
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317003	A1	19930902	WO 1993-US1785	19930226
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9337357	A1	19930913	AU 1993-37357	19930226
EP 628035	A1	19941214	EP 1993-906262	19930226
R: BE, CH, DE, FR, GB, IT, NL				
JP 07504417	T2	19950518	JP 1993-515105	19930226
PRIORITY APPLN. INFO.:			US 1992-842295	19920226
			US 1992-842299	19920226
			WO 1993-US1785	19930226

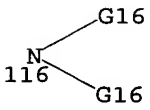
AB The title compds. R1(R5)CHCH(OH)CH(R2)CH(R3)R4 [R1, R3 = H, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, etc.; R2 = H, OH; R4 = (un)substituted amino, (un)substituted carbonylamino; R5 = (un)substituted amino, heterocyclyl-substituted amino], which inhibit HIV retroviral protease and which are useful in the treatment of retrovirus infections, are prepared and title compound-containing formulations are presented. Thus, (2R,4S,5S, 1'S)-6-phenyl-5-(tert-butyloxycarbonyl) amino-4-hydroxy-N-[1'-isopropyl-1'-(1,2,4-triazol-3-yl)]methyl-2-phenylmethylhexanamide, which was prepared from N-benzyloxycarbonyl-valinamide in four steps, demonstrated 50% inhibitory concentration against HIV-infected cells of <2 μM and had a Ki of <10 nM for the inhibition of HIV-1 protease enzyme.

MSTR 6

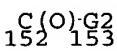


G1 = OPh (opt. substd.)
G7 = bond
G8 = 143 / 150

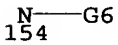
G16 = Ph
G24 = carbon chain <0 or more double bonds, 0 or more triple bonds> (opt. substd. by 1 or more G25)
G25 = 116 / OH (opt. substd.)



G28 = 152-1 153-151



G29 = 154



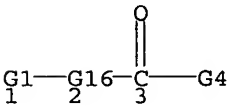
Patent location: claim 11
Note: any reactive group is protected

L43 ANSWER 24 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 118:81438 MARPAT <<LOGINID::20061206>>
TITLE: Peptide keto amides, keto acids, and keto esters
INVENTOR(S): Powers, James C.
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

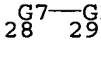
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9212140	A1	19920723	WO 1991-US9801	19911227
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2098702	AA	19920629	CA 1991-2098702	19911227
AU 9191553	A1	19920817	AU 1991-91553	19911227
AU 654834	B2	19941124		
EP 564561	A1	19931013	EP 1992-903265	19911227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL				
PRIORITY APPLN. INFO.:			US 1990-635287	19901228
			WO 1991-US9801	19911227

AB Title compds. R-X-X1-COR1 [X, X1 = amino acids; R = H, (un)substituted H2NCO, H2NCS, H2NSO2, amino acid; R1 = alkoxy, OH, (un)substituted NH2] were prepared as serine and cysteine protease inhibitors. Thus, Z-Leu-Phe-OH (Z = CO2CH2Ph) was treated with ClCOCO2Et in the presence of 4-dimethylaminopyridine to give Z-Leu-NHC(CH2Ph)=C(CO2Et)O2CCO2Et which was hydrolyzed to 2-Leu-Phe-CO2Et. The latter compound was ketalized and amidated with EtNH2, to give Z-Leu-Phe-CONHEt (I). I inhibited calpain from humor erythrocytes at 7 μm.

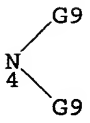
MSTR 5



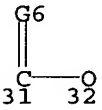
G1 = 28



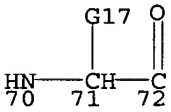
G3 = 1-adamantyl
G4 = 4



G6 = O
G7 = 31-2 32-29



G9 = alkyl <containing 1-20 C>
(opt. substd. by Ph (opt. substd.))
G16 = 70-1 72-3



G17 = Me
Derivative: or protected derivatives
Derivative: or pharmaceutically acceptable salts
Patent location: claim 5
Note: also incorporates claims 8 and 13
Stereochemistry: 71,76,116,145,151,158-D,L

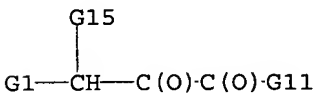
L43 ANSWER 25 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 117:212981 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of peptides containing β-amino-α-ketoacid groups as protease inhibitors
INVENTOR(S): Yamada, Fumika; Sugimura, Hideo; Someno, Tetsuya; Muraoka, Yasuhiko; Tsuda, Makoto; Takeuchi, Tomio; Aoyanagi, Takaaki
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04149166	A2	19920522	JP 1990-272183	19901012

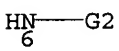
PRIORITY APPLN. INFO.: JP 1990-272183 19901012
AB XNHCHRCOCOY [I; X = H, amino, (un)protected peptide or amino acid residue; Y = (un)protected peptide or amino acid residue; R = (un)substituted Ph or naphthyl] are prepared as protease inhibitors (no data). Thus, N-acylation

of threo-3-amino-2-hydroxy-4-(o-methoxyphenyl)butyric acid with di-tert-Bu dicarbonate in 1N NaOH and dioxane and condensation of the resultant threo-3-tert-butoxycarbonylamino-2-hydroxy-4-(o-methoxyphenyl)butyric acid (64.5% yield) with H-D-Val-Val-OCH2Ph.CF3CO2H in the presence of 1-hydroxybenzotriazole and DCC in CH2Cl2 gave 80.5% N-[(3RS)-3-tert-butoxycarbonylamino-2-hydroxy-4-(o-methoxyphenyl)butanoyl]-D-leucyl-L-valine benzyl ester which was oxidized with pyridine trifluoroacetate, DCC, and DMSO in benzene to give 73.1% N-[(3RS)-3-tert-butoxycarbonylamino-2-oxo-4-(o-methoxyphenyl)butanoyl]-D-leucyl-L-valine benzyl ester. A total of 18 I were prepared

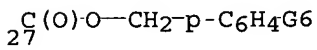
MSTR 1A



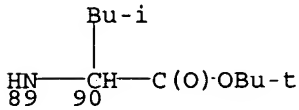
G1 = 6



G2 = 27



G11 = 89

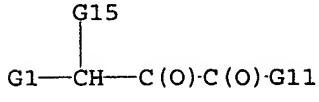


G15 = loweralkyl (substd. by Ph (substd. by 1 or more G16))

Patent location: claim 1

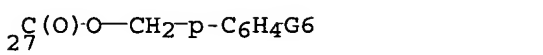
Stereochemistry: 79-D; 90-D

MSTR 1B

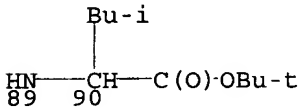


G1 = 6

G2 = 27

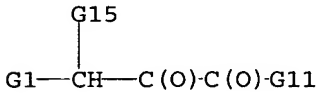


G11 = 89



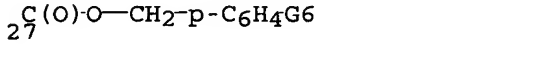
G15 = loweralkyl (substd. by G17)
Patent location: claim 1
Stereochemistry: 79-D; 90-D

MSTR 1C

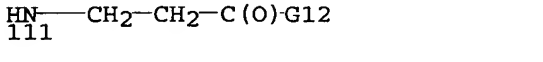


G1 = 6

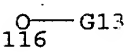
G2 = 27



G11 = 111

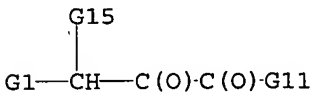


G12 = 116

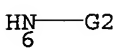


G13 = Me
G15 = loweralkyl (substd. by G17)
Patent location: claim 1

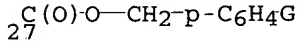
MSTR 1D



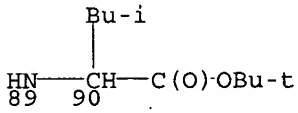
G1 = 6



G2 = 27

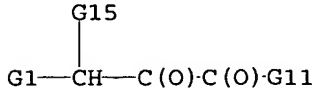


G11 = 89



G15 = loweralkyl (substd. by G17)
Patent location: claim 1
Stereochemistry: 79-D; 90-D

MSTR 1E



G1 = 6

HN(6)—G2

G2 = 27

C(27)(O)-O—CH_2-p-C_6H_4G6

G11 = 111

HN(111)—CH_2—CH_2—C(O)-G12

G12 = 116

O(116)—G13

G13 = Me
G15 = loweralkyl (substd. by G17)
Patent location: claim 1

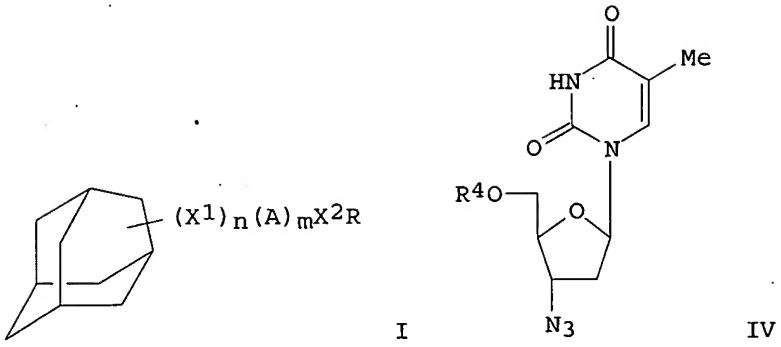
L43 ANSWER 26 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 117:49260 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of adamantylated peptides and other drugs with high blood-brain barrier permeability
INVENTOR(S): Kitagawa, Kouki; Hibi, Toru; Tsuzuki, Noriko
PATENT ASSIGNEE(S): Teikoku Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9113081	A1	19910905	WO 1991-JP256	19910227
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
EP 516851	A1	19921209	EP 1991-905340	19910227
EP 516851	B1	19960619		
R: CH, DE, DK, FR, GB, LI, SE				
EP 668290	A1	19950823	EP 1995-105215	19910227
EP 668290	B1	19981111		
R: CH, DE, DK, FR, GB, LI, SE				
US 5652335	A	19970729	US 1994-227997	19940415

PRIORITY APPLN. INFO.: JP 1990-50116 19900228
EP 1991-905340 19910227
WO 1991-JP256 19910227

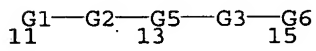
US 1992-920582 19920828

GI

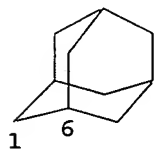


AB The title compds. (I; X1, X2 = ether, urethane, ester, amide bond; A = lower alkylene; when m = 0, n = 0, or when m = 1, n = 0 or 1; R = residue of a physiol. active substance selected from peptides, amino acids, aliphatic amines having a phenolic skeleton, amino sugars, nucleosides, lactam compds., and their derivs., particularly enkephalin, zidovudine, or 2-pyrrolidone), which show high blood-brain barrier permeability and are useful as pharmaceuticals active to the brain, are prepared Thus, hydrogenolysis of Z-Phe-Leu-NHAda (Ada = 1-adamantyl, Z = PhCH2OC) (preparation given) over 5% Pd/C in THF containing AcOH followed by condensation of the azide prepared from Z-Tyr(Bzl)-D-Ala-Gly-R2 (II; R2 = NHNH2, Bzl = PhCH2) (preparation given) in the presence of Et3N in DMF at 0° gave 81% II (R2 = Phe-Leu-NHAda) which was similarly hydrogenolyzed to give 41% H-Tyr-D-Ala-Gly-Phe-Leu-R3 (III; R3 = NHAda). This in vitro was 2.13 times as potent as morphine-HCl in inhibiting the contraction of guinea pigs intestinal tract in the Kosterlitz's assay. Also prepared were III (R3 = OAda, OCH2Ada, OCH2CH2Ada), zidovudine derivs. (IV; R4 = AdaCO, etc.), and (adamantanecarbonyl)pyrrolidone.

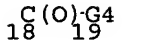
MSTR 1A



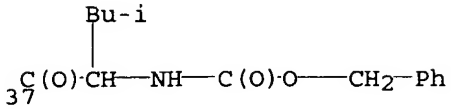
G1 = 1 / 6



G2 = bond
G3 = 18-13 19-15 / 19-13 18-15

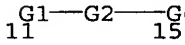


G4 = NH
G5 = loweralkylene
G6 = 37

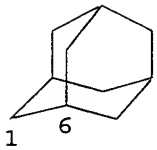


Patent location: claim 1
Stereochemistry: 24-D

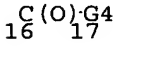
MSTR 1B



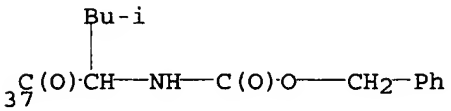
G1 = 1 / 6



G2 = 16-11 17-15 / 17-11 16-15



G4 = NH
G6 = 37



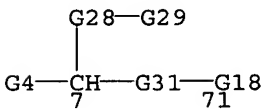
Patent location: claim 1
Stereochemistry: 24-D

L43 ANSWER 27 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 113:153045 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of retroviral protease-inhibiting peptides and pharmaceutical compositions containing them
INVENTOR(S): Dreyer, Geoffrey Bainbridge; Huffman, William Francis; Meek, Thomas Dowing; Metcalf, Brian Walter; Moore, Michael Lee
PATENT ASSIGNEE(S): SmithKline Beckman Corp., USA
SOURCE: Eur. Pat. Appl., 118 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

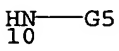
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 352000	A2	19900124	EP 1989-306995	19890710
EP 352000	A3	19910717		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8905174	A	19900328	ZA 1989-5174	19890707
CN 1039596	A	19900214	CN 1989-104699	19890708
PRIORITY APPLN. INFO.:			US 1988-216178	19880708
			US 1989-321937	19890310

AB A-B-(Q)a-(C)b-(D)c-M-(W)d-(X)e-Y-Z [I; A = H, protecting group, (protected) amino, alkanamido, etc.; B = D- or L-amino acid residue, e.g., β-Ala, bond; C, D = Glx, Asx, Ala, β-Ala, Arg, Gly, Ile, Leu, Lys, Ser, Thr, Val, Met, His; Asx = Asp, Asn; Glx = Glu, Gln; Q = D- or L-amino acid residue, e.g.; Ser, Thr, Asp, His, Cys, Arg, Ala; W = Pro, dehydro-Pro; X = Ala, Gly, Ile, Leu, Val, Met, Lys, Glx, Asx; Y = D- or L-amino acid residue(s), bond; Z = CO2H, alkoxycarbonyl, (substituted) amino, etc.; a-e = 0, 1, however, c and e may not simultaneously be 0; M = Cha, (substituted) Phe, alkylamino] and their pharmaceutically acceptable salts were prepared Many I, e.g., Ac-Ser-Gln-Ser-Tyr-Pro-Val-Val-NH2, were prepared by solid-phase or solution synthesis. 2-(Acetylserylglutaminylasparaginyl)amino-3-phenylpropylprolylvalylvalinamide (preparation given) showed an inhibition constant Ki of 14 μM in vitro against rHIV protease. Many pharmaceutical dosage forms containing 1 were formulated.

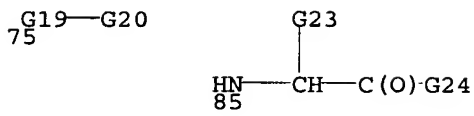
MSTR 1G



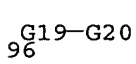
G4 = 10



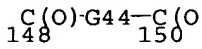
G5 = CO2CH2Ph
G18 = 75 / 85



G19 = O
G20 = alkyl <containing 1-5 C>
G24 = 96

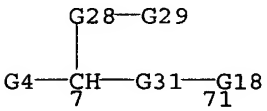


G28 = alkylene <containing 1-5 C>
G31 = 148-7 150-71

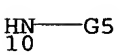


G44 = bond
Derivative: and pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

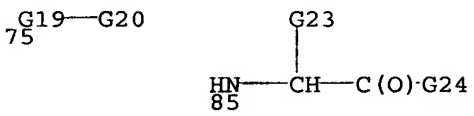
MSTR 1I



G4 = 10



G5 = CO2CH2Ph
G18 = 75 / 85



G19 = O
G20 = alkyl <containing 1-5 C>

G24 = 96

G19—G20
96

G28 = alkylene <containing 1-5 C>
G31 = 148-7 150-71

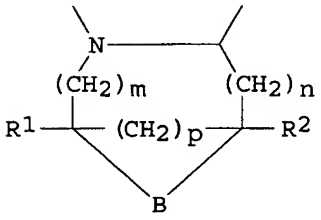
C(O)-G44—C(O)
148 150

G44 = bond
Derivative: and pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

L43 ANSWER 28 OF 28 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 111:39867 MARPAT <<LOGINID::20061206>>
TITLE: Preparation of tripeptides containing a polycyclic amine and pharmaceutical compositions containing them
INVENTOR(S): Vincent, Michel; Remond, Georges; Portevin, Bernard; Cudennec, Claude
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 296059	A1	19881221	EP 1988-401476	19880615
EP 296059	B1	19920318		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2616663	A1	19881223	FR 1987-8350	19870616
FR 2616663	B1	19890818		
AU 8817741	A1	19881222	AU 1988-17741	19880615
AU 612657	B2	19910718		
JP 01019096	A2	19890123	JP 1988-147930	19880615
JP 06037518	B4	19940518		
ZA 8804276	A	19890329	ZA 1988-4276	19880615
AT 73822	E	19920415	AT 1988-401476	19880615
ES 2032985	T3	19930301	ES 1988-401476	19880615
DK 8803305	A	19881217	DK 1988-3305	19880616
US 5047400	A	19910910	US 1988-207710	19880616
CA 1336349	A1	19950718	CA 1988-569700	19880616
PRIORITY APPLN. INFO.:			FR 1987-8350	19870616
			EP 1988-401476	19880615

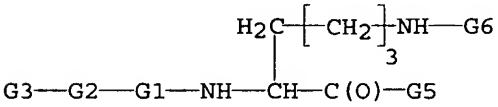
GI



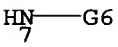
Q

AB RCHYC(:X)-Lys-X1-CO-Arg-OH [I; X = O, H2; Y = H, OH, NH2 (when X = H2); R = H, alkyl; X1 = Q; R1, R2 = H, or R1R2 = bond when p = 0; m = 1, 0; n, p = 1,2; B = (CH2)g (when g = 2,3,4), (CH:CH)2 (when p = O, R1R2 = bond, and m + n + p + q = an integer between 3 and 60), 1,2,3,4-tetrahydrocarboline residue], their enantiomers, epimers, diastereoisomers, and their pharmaceutically acceptable salts, useful as aminopeptidase inhibitors and immunostimulants, are prepared via condensing RCJKC(:X)R3 [R3 = H, OH (when X = O), H, Br (when X = H2); J = H, OH (when K = H), benzyloxycarbonylamino (when K = R3 = H), etc.] with Z-Lys-OCMe3 (Z = benzyloxycarbonyl) followed by deprotection, peptide coupling, deprotection, etc. (2S,3R)-AHPA-(S)-Lys-(S)-PHI-(S)-Arg-OH [AHPA = 2-hydroxy-3-amino-4-phenylbutanoic acid residue; (S)-PHI = perhydroindole-2-carboxylic acid residue] was prepared by peptide coupling of BOC-(S)-PHI-OH with the appropriately protected arginine benzyl ester, deprotection, coupling the product with Z-(2S,3R)-APHA-(S)-Lys-O-CMe3 (prepared given), and deprotection. An in vitro study using peritoneal macrophages of mice showed that I in general augmented their phagocytosis by 25%.

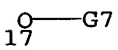
MSTR 4



G1 = C(O)
G2 = C(O)
G3 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4)
G4 = 7

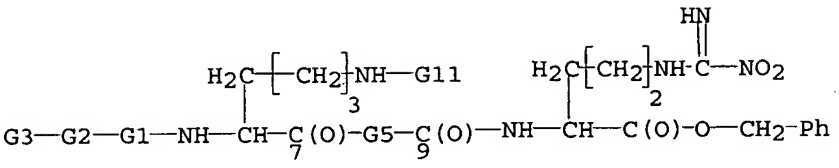


G5 = 17

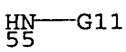


G6 = CO2CH2Ph
G7 = Bu-t
Patent location: claim 11

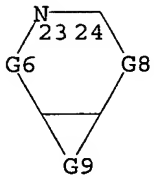
MSTR 7A



G1 = C(O)
G2 = C(O)
G3 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4)
G4 = 55

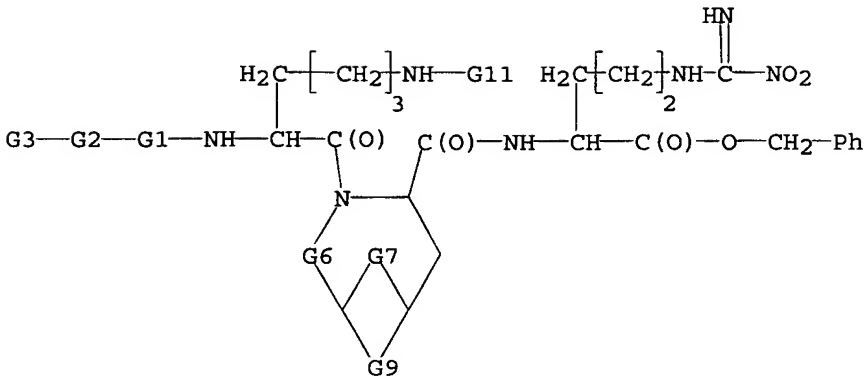


G5 = 23-7 24-9

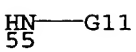


G6 = bond
G8 = bond
G9 = CH2CH2
G11 = CO2CH2Ph
Patent location: claim 11

MSTR 7B

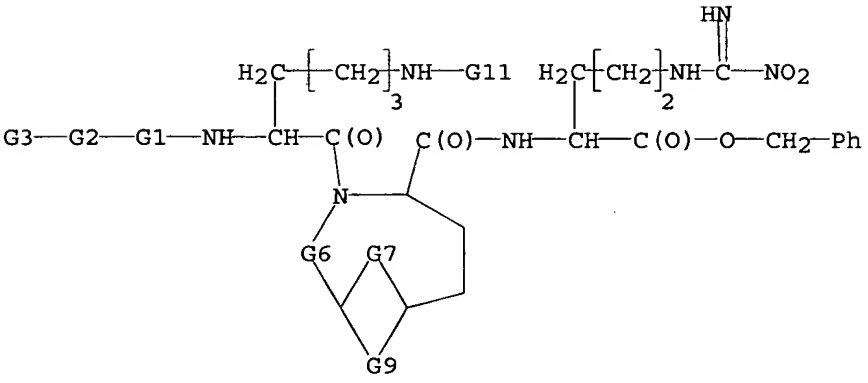


G1 = C(O)
G2 = C(O)
G3 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4)
G4 = 55



G6 = bond
G7 = CH2
G9 = CH2CH2
G11 = CO2CH2Ph
Patent location: claim 11

MSTR 7C



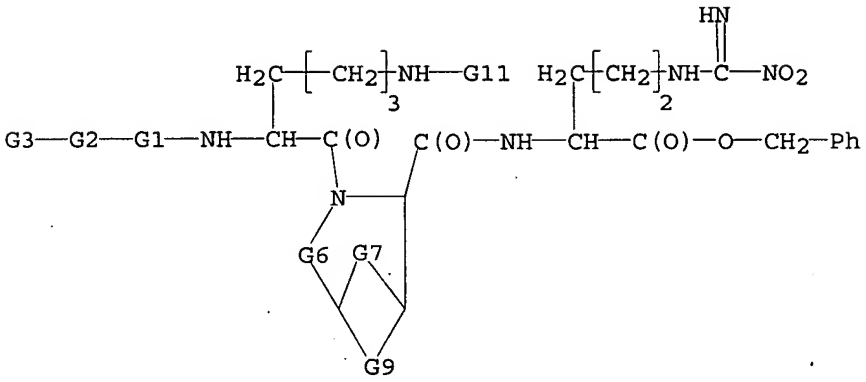
G1 = C(O)
G2 = C(O)
G3 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4)

G4 = 55

HN——G11
55

G6 = bond
G7 = CH2
G9 = CH2CH2
G11 = CO2CH2Ph
Patent location: claim 11

MSTR 7D



G1 = C(O)
G2 = C(O)
G3 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4)
G4 = 55

HN——G11
55

G6 = bond
G7 = CH2
G9 = CH2CH2
G11 = CO2CH2
Patent location

Only 1 compound is printed per references of file Mabs.

=> file beils
FILE 'BEILSTEIN' 06 DEC 2006
COPYRIGHT (c) 2 ur Foerderung der Chemischen Wissenschaften
licensed to Beilstein GmbH and MDL Information Systems GmbH

FILE LAST UPDATED ON JUNE 16, 2006

FILE COVERS 1771 TO 2006.
*** FILE CONTAINS 9,606,495 SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

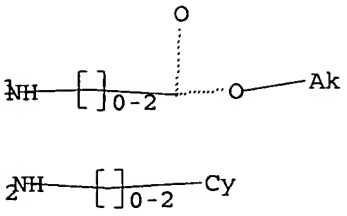
>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

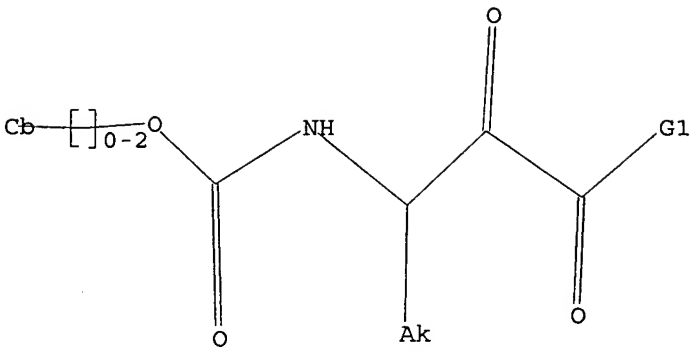
****
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *
****

NEW

* ***PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.***
* ***NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.***

=> d que l39
L1 STR





G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

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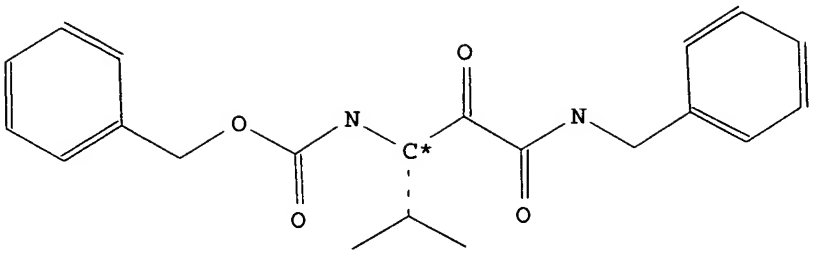
L27	75	SEA FILE=BEILSTEIN	SSS FUL L1		
L28	75	SEA FILE=BEILSTEIN	ABB=ON	PLU=ON	L27 NOT L7
L29	72	SEA FILE=BEILSTEIN	ABB=ON	PLU=ON	L28 AND BABSAN/FA
L39	3	SEA FILE=BEILSTEIN	ABB=ON	PLU=ON	L28 NOT L29

=> d ide allref l39 tot

L39 ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	10101574
Chemical Name (CN):	(1-benzylaminooxalyl-2-methyl-propyl)-carbamic acid benzyl ester
Autonom Name (AUN):	(1-benzylaminooxalyl-2-methyl-propyl)-carbamic acid benzyl ester
Molec. Formula (MF):	C21 H24 N2 O4
Molecular Weight (MW):	368.43
Lawson Number (LN):	14140, 5228, 3610, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	8491515
Tautomer ID (TAUTID):	9469017
Entry Date (DED):	2006/02/02
Update Date (DUPD):	2006/02/02



Field Availability:

Code	Name	Occurrence
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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

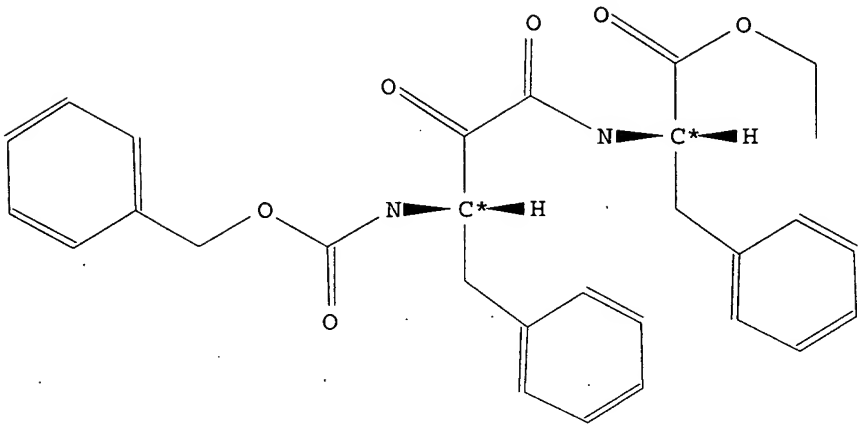
All References:
ALLREF

1. Choe, Youngchool; Brinen, Linda S.; Price, Mark S.; Engel, Juan C.; Lange, Meinolf; Grisostomi, Corinna; Weston, Scott G.; Pallai, Peter V.; Cheng, Hong; Hardy, Larry W.; Hartsough, David S.; et al., Bioorg. Med. Chem., CODEN: BMECEP, 13(6), <2005>, 2141 - 2156; BABS-6507298

L39 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	6947092
Chemical Name (CN):	2-(3-benzyloxycarbonylamino-2-oxo-4-phenyl-butyrylamino)-3-phenyl-propionic acid ethyl ester
Autonom Name (AUN):	2-(3-benzyloxycarbonylamino-2-oxo-4-phenyl-butyrylamino)-3-phenyl-propionic acid ethyl ester
Molec. Formula (MF):	C29 H30 N2 O6
Molecular Weight (MW):	502.57
Lawson Number (LN):	16298, 16048, 5228, 1762, 298

File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	6003567
Tautomer ID (TAUTID):	6618828
Beilstein Citation (BSO):	6-14
Entry Date (DED):	1995/01/25
Update Date (DUPD):	1995/01/25



Field Availability:

Code	Name	Occurrence
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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

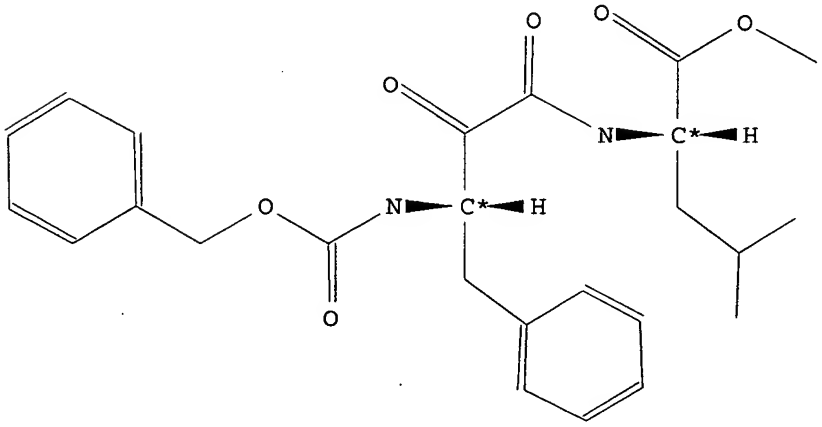
Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Wasserman, Harry H.; Ho, Wen-Bin, J.Org.Chem., CODEN: JOCEAH, 59(16), <1994>, 4364-4366; BABS-5909301

L39 ANSWER 3 OF 3 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	6945599
Chemical Name (CN):	2-(3-benzyloxycarbonylamino-2-oxo-4-phenyl-butyrylamino)-4-methyl-pentanoic acid methyl ester
Autonom Name (AUN):	2-(3-benzyloxycarbonylamino-2-oxo-4-phenyl-butyrylamino)-4-methyl-pentanoic acid methyl ester
Molec. Formula (MF):	C25 H30 N2 O6
Molecular Weight (MW):	454.52
Lawson Number (LN):	16298, 5228, 3409, 1762, 289
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	5999589
Tautomer ID (TAUTID):	6614986
Beilstein Citation (BSO):	6-14
Entry Date (DED):	1995/01/25
Update Date (DUPD):	1995/01/25



Field Availability:

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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1

BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Wasserman, Harry H.; Ho, Wen-Bin, J.Org.Chem., CODEN: JOCEAH, 59(16), <1994>, 4364-4366; BABS-5909301

=> d que l38
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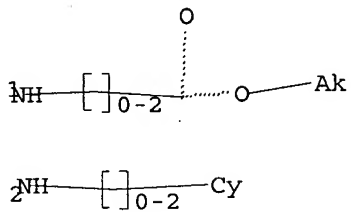

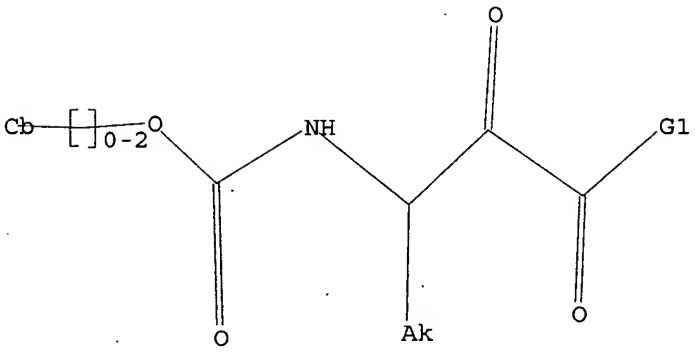

G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

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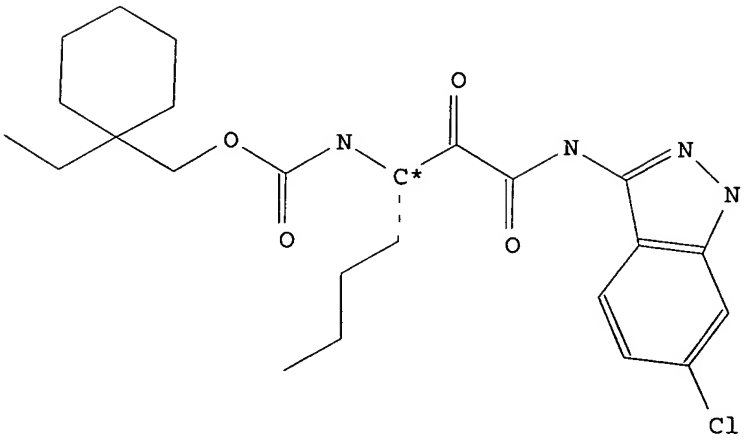
L27	75	SEA FILE=BEILSTEIN SSS FUL L1
L28	75	SEA FILE=BEILSTEIN ABB=ON PLU=ON L27 NOT L7
L29	72	SEA FILE=BEILSTEIN ABB=ON PLU=ON L28 AND BABSAN/FA
L38	25	SEA FILE=BEILSTEIN ABB=ON PLU=ON L29 AND 6470649/BABSAN

=> d ide allref l38 1

L38 ANSWER 1 OF 25 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	9884499
Chemical Name (CN):	(1-ethylcyclohexyl)methyl (1S)-1-<<(6-chloro-1H-indazol-3-yl)amino>(oxo)acetyl>pentylcarbamate
Autonom Name (AUN):	<1-(6-chloro-1H-indazol-3-ylaminooxalyl)-pentyl>-carbamic acid 1-ethyl-cyclohexylmethyl ester
Molec. Formula (MF):	C24 H33 Cl N4 O4
Molecular Weight (MW):	477.00
Lawson Number (LN):	29567, 5031, 3610, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8321654
Tautomer ID (TAUTID):	9253650
Entry Date (DED):	2005/04/22
Update Date (DUPD):	2005/04/22



Field Availability:

Code	Name	Occurrence
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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1

DED	Entry Date	1
DUPD	Update Date	1
NMR	Nuclear Magnetic Resonance	2
PHARM	Pharmacological Data	4

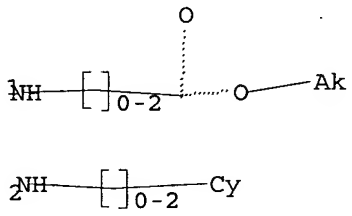
This substance also occurs in Reaction Documents:

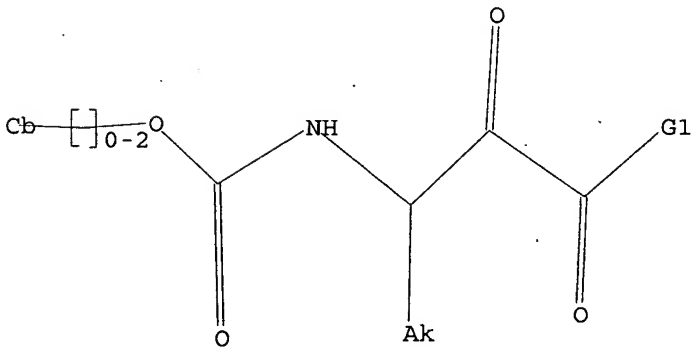
Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Tavares, Francis X.; Deaton, David N.; Miller, Aaron B.; Miller, Larry R.; Wright, Lois L.; Zhou, Hui-Qiang, J. Med. Chem., CODEN: JMCMAR, 47(21), <2004>, 5049 - 5056; BABS-6470649

=> d que l37
L1 STR





G1 [@1], [@2]

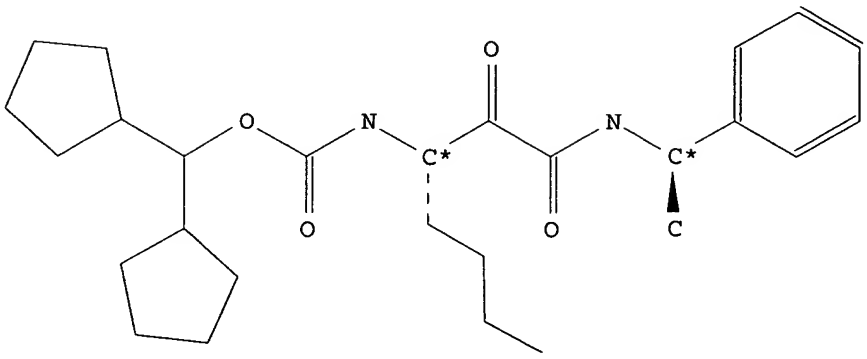
Structure attributes must be viewed using STN Express query preparation.

L7	98	SEA FILE=REGISTRY SSS FUL L1
L27	75	SEA FILE=BEILSTEIN SSS FUL L1
L28	75	SEA FILE=BEILSTEIN ABB=ON PLU=ON L27 NOT L7
L29	72	SEA FILE=BEILSTEIN ABB=ON PLU=ON L28 AND BABSAN/FA
L37	1	SEA FILE=BEILSTEIN ABB=ON PLU=ON L29 AND 6437071/BABSAN

=> d ide allref l37 1

L37 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	9669935
Chemical Name (CN):	<1-(1-phenyl-ethylaminooxalyl)-pentyl>-carbamic acid dicyclopentylmethyl ester
Autonom Name (AUN):	<1-(1-phenyl-ethylaminooxalyl)-pentyl>-carbamic acid dicyclopentylmethyl ester
Molec. Formula (MF):	C27 H40 N2 O4
Molecular Weight (MW):	456.62
Lawson Number (LN):	14150, 5120, 3610, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	8148728
Tautomer ID (TAUTID):	9070329
Entry Date (DED):	2004/07/21
Update Date (DUPD):	2004/07/21



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Catalano, John G.; Deaton, David N.; Long, Stacey T.; McFadyen, Robert B.; Miller, Larry R.; Payne, J. Alan; Wells-Knecht, Kevin J.; Wright, Lois L., Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 14(3), <2004>, 719 - 722; BABS-6437071

=> d que l36
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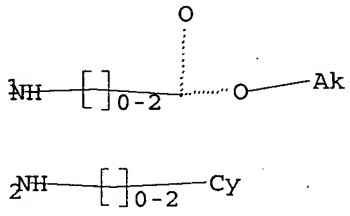
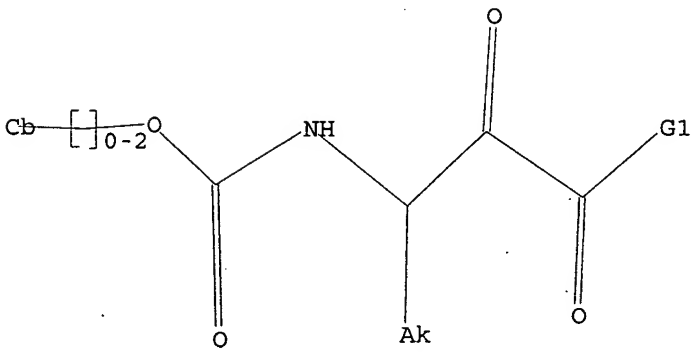




G1 [@1], [@2]

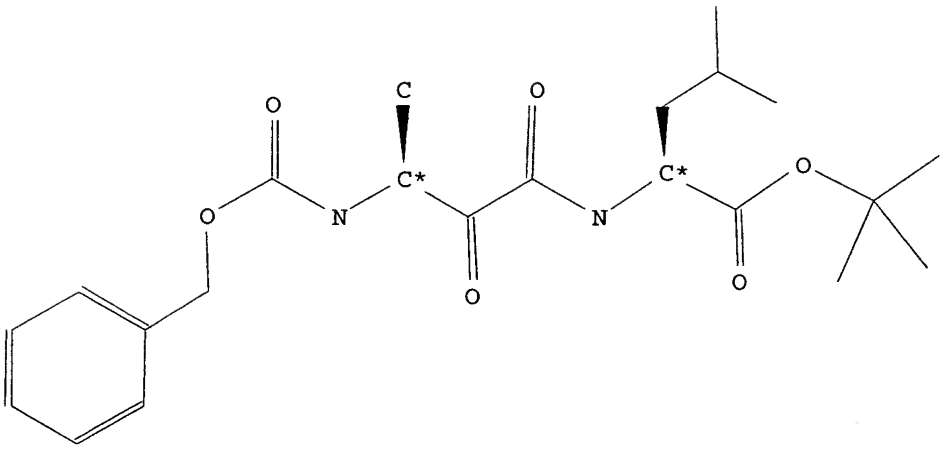
Structure attributes must be viewed using STN Express query preparation.

L7	98	SEA FILE=REGISTRY SSS FUL L1	
L27	75	SEA FILE=BEILSTEIN SSS FUL L1	
L28	75	SEA FILE=BEILSTEIN ABB=ON PLU=ON	L27 NOT L7
L29	72	SEA FILE=BEILSTEIN ABB=ON PLU=ON	L28 AND BABSAN/FA
L36	1	SEA FILE=BEILSTEIN ABB=ON PLU=ON	L29 AND 6410184/BABSAN

=> d ide allref l36 1

L36 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	7891902
Chemical Name (CN):	2-(3-benzyloxycarbonylamino-2-oxobutyrylamino)-4-methylpentanoic acid tert-butyl ester
Autonom Name (AUN):	2-(3-benzyloxycarbonylamino-2-oxo-butyrylamino)-4-methyl-pentanoic acid tert-butyl ester
Molec. Formula (MF):	C22 H32 N2 O6
Molecular Weight (MW):	420.50
Lawson Number (LN):	5228, 3615, 3409, 1762, 318
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	6703258
Tautomer ID (TAUTID):	7440363
Beilstein Citation (BSO):	6-06
Entry Date (DED):	1998/07/15
Update Date (DUPD):	2004/01/21



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1

BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1
CPD	Crystal Property Description	1
IR	Infrared Spectrum	1
MS	Mass Spectrum	1
NMR	Nuclear Magnetic Resonance	3
ORP	Optical Rotatory Power	1

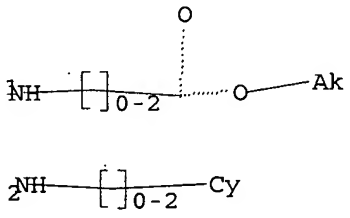
This substance also occurs in Reaction Documents:

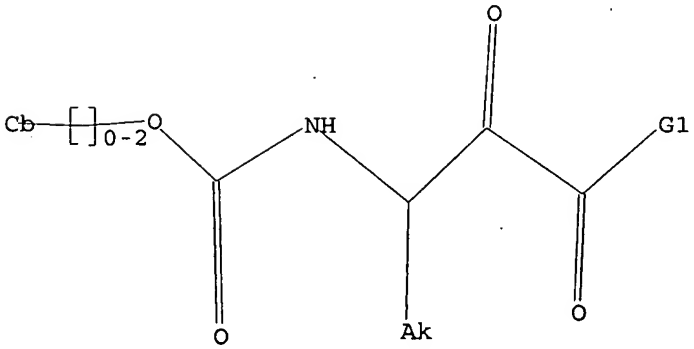
Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Wasserman, Harry H.; Petersen, Anders K.; Xia, Mingle, Tetrahedron, CODEN: TETRAB, 59(35), <2003>, 6771 - 6784; BABS-6410184
2. Wasserman, Harry H.; Petersen, Anders K., J.Org.Chem., CODEN: JOCEAH, 62(26), <1997>, 8972-8973; BABS-6080022

=> d que l35
L1 STR





G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

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L27           75 SEA FILE=BEILSTEIN SSS FUL L1
L28           75 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L27 NOT L7
L29           72 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L28 AND BABSAN/FA
L35            0 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L29 AND 6080022/BABSAN


=> d que l34
L1              STR
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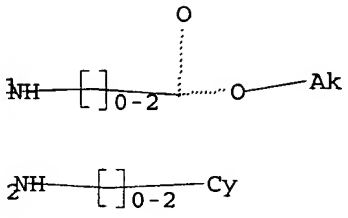

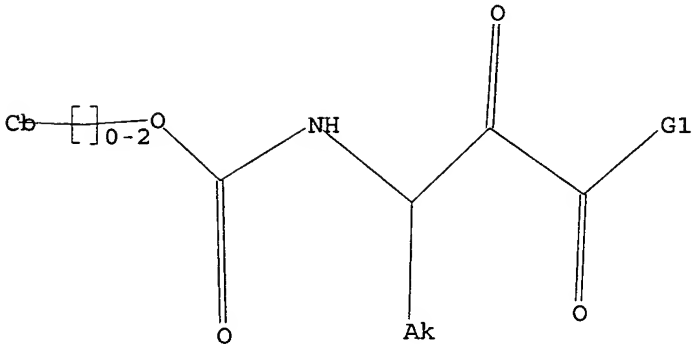

G1 [@1], [@2]

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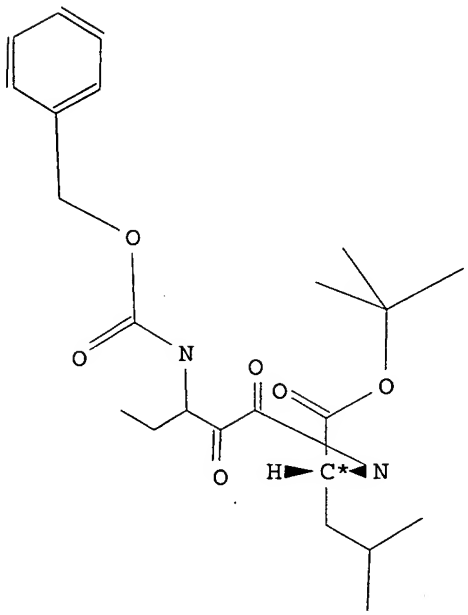
Structure attributes must be viewed using STN Express query preparation.
L7            98 SEA FILE=REGISTRY SSS FUL L1
L27           75 SEA FILE=BEILSTEIN SSS FUL L1
L28           75 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L27 NOT L7
L29           72 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L28 AND BABSAN/FA
L34            1 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L29 AND 6021920/BABSAN


=> d ide allref l34 1


L34  ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

     Beilstein Records (BRN):        7553145
     Chemical Name (CN):             2-(3-benzyloxycarbonylamino-2-oxo-
                                     pentanoylamino)-4-methyl-pentanoic acid
                                     tert-butyl ester
     Autonom Name (AUN):             2-(3-benzyloxycarbonylamino-2-oxo-
                                     pentanoylamino)-4-methyl-pentanoic acid
                                     tert-butyl ester
```

Molec. Formula (MF):	C23 H34 N2 O6
Molecular Weight (MW):	434.53
Lawson Number (LN):	5228, 3608, 3409, 1762, 318
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	6455279
Tautomer ID (TAUTID):	7161326
Beilstein Citation (BSO):	6-06
Entry Date (DED):	1997/02/02
Update Date (DUPD):	1997/11/18



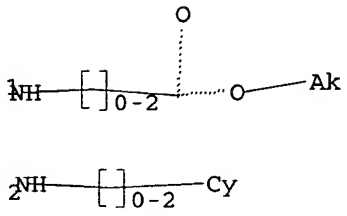
Field Availability:

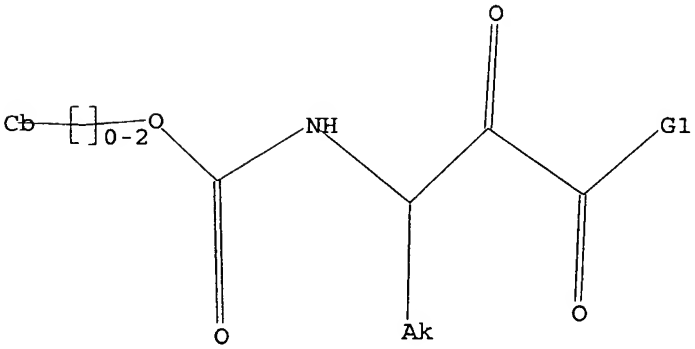
Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	1

All References:
ALLREF

1. Tsuda, Makoto; Muraoka, Yasuhiko; Someno, Tetsuya; Nagai, Machiko; Aoyagi, Takaaki; Takeuchi, Tomio, J.Antibiot., CODEN: JANTAJ, 49(9), <1996>, 900-908; BABS-6021920

=> d que l33
L1 STR





G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

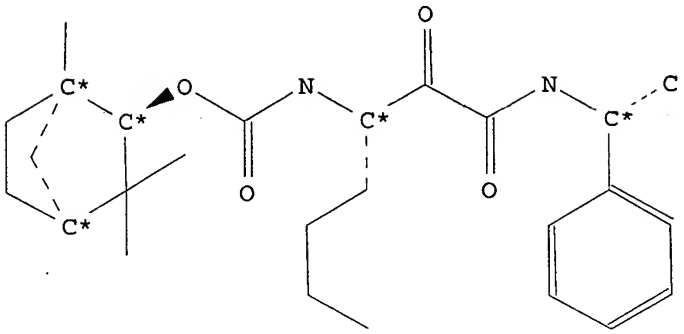
L7	98	SEA	FILE=REGISTRY	SSS FUL	L1
L27	75	SEA	FILE=BEILSTEIN	SSS FUL	L1
L28	75	SEA	FILE=BEILSTEIN	ABB=ON PLU=ON	L27 NOT L7
L29	72	SEA	FILE=BEILSTEIN	ABB=ON PLU=ON	L28 AND BABSAN/FA
L33	7	SEA	FILE=BEILSTEIN	ABB=ON PLU=ON	L29 AND 6498996/BABSAN

=> d ide allref l33 1

L33 ANSWER 1 OF 7 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	10038966
Chemical Name (CN):	<1-(1-phenyl-ethylaminooxalyl)-pentyl>-carbamic acid 1,3,3-trimethyl-bicyclo<2.2.1>hept-2-yl ester
Autonom Name (AUN):	<1-(1-phenyl-ethylaminooxalyl)-pentyl>-

	carbamic acid 1,3,3-trimethyl-bicyclo<2.2.1>hept-2-yl ester
Molec. Formula (MF):	C26 H38 N2 O4
Molecular Weight (MW):	442.60
Lawson Number (LN):	14150, 5114, 3610, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	8440425
Tautomer ID (TAUTID):	9399766
Entry Date (DED):	2005/10/20
Update Date (DUPD):	2005/10/20



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	6

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Barrett, David G.; Catalano, John G.; Deaton, David N.; Long, Stacey T.; McFadyen, Robert B.; Miller, Aaron B.; Miller, Larry R.; Wells-Knecht, Kevin J.; Wright, Lois L., Bioorg. Med. Chem. Lett., CODEN: BMCLE8, 15(9), <2005>, 2209 - 2214; BABS-6498996

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=> d que l32
L1              STR
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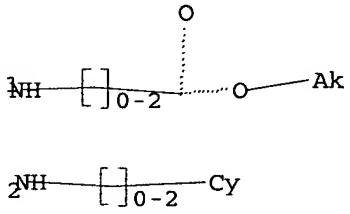

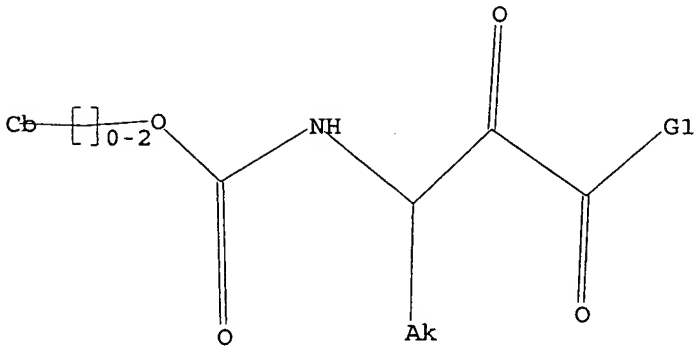

G1 [@1], [@2]

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Structure attributes must be viewed using STN Express query preparation.
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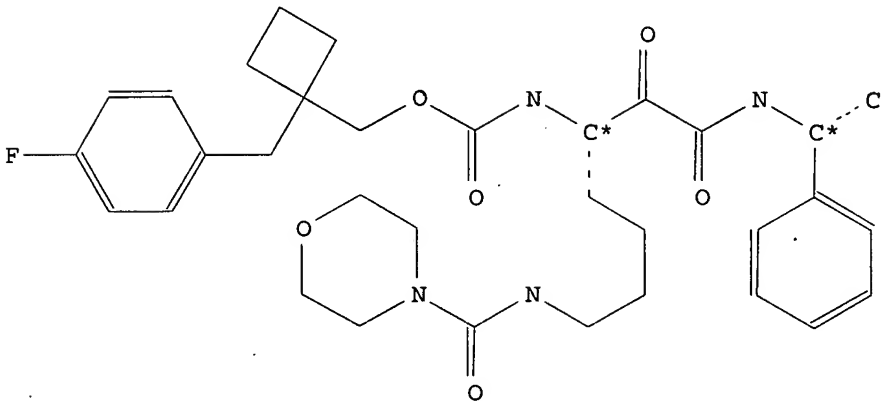
L27           75 SEA FILE=BEILSTEIN SSS FUL L1
L28           75 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L27 NOT L7
L29           72 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L28 AND BABSAN/FA
L32           15 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L29 AND 6462233/BABSAN

=> d ide allref l32 1

L32  ANSWER 1 OF 15 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

     Beilstein Records (BRN):        9829356
     Chemical Name (CN):             <5-<(morpholine-4-carbonyl)-amino>-1-(1-
                                     phenyl-ethylaminooxalyl)-pentyl>-carbamic
                                     acid 1-(4-fluoro-benzyl)-cyclobutylmethyl
                                     ester
     Autonom Name (AUN):             <5-<(morpholine-4-carbonyl)-amino>-1-(1-
                                     phenyl-ethylaminooxalyl)-pentyl>-carbamic
```

	acid 1-(4-fluoro-benzyl)-cyclobutylmethyl ester
Molec. Formula (MF):	C33 H43 F N4 O6
Molecular Weight (MW):	610.72
Lawson Number (LN):	30824, 14150, 5368, 3610, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8279024
Tautomer ID (TAUTID):	9208586
Entry Date (DED):	2005/01/21
Update Date (DUPD):	2005/01/21



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	8

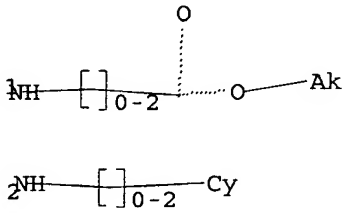
This substance also occurs in Reaction Documents:

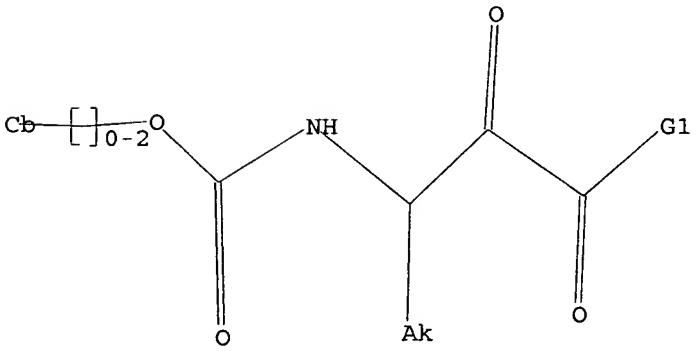
Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Barrett, David G.; Catalano, John G.; Deaton, David N.; Hassell, Anne M.; Long, Stacey T.; Miller, Aaron B.; Miller, Larry R.; Shewchuk, Lisa M.; Wells-Knecht, Kevin J.; Willard, Derril H.; Wright, Lois L., Bioorg. Med. Chem. Lett., CODEN: BMCLE8, 14(19), <2004>, 4897 - 4902; BABS-6462233

=> d que l31
L1 STR





G1 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

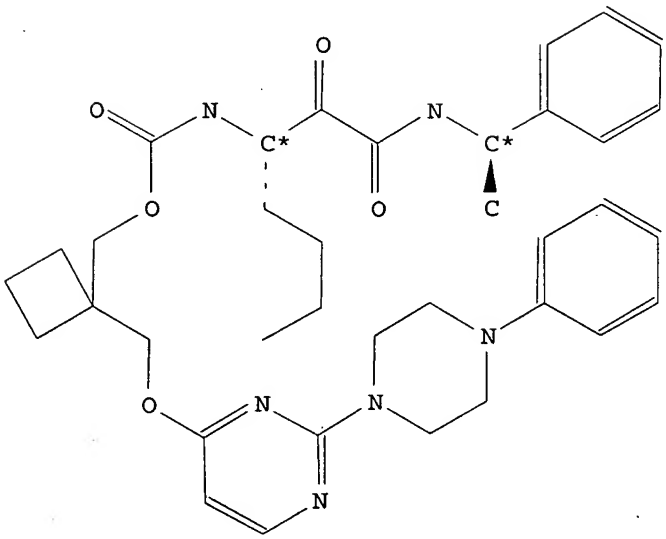
L7	98	SEA FILE=REGISTRY SSS FUL L1
L27	75	SEA FILE=BEILSTEIN SSS FUL L1
L28	75	SEA FILE=BEILSTEIN ABB=ON PLU=ON L27 NOT L7
L29	72	SEA FILE=BEILSTEIN ABB=ON PLU=ON L28 AND BABSAN/FA
L31	22	SEA FILE=BEILSTEIN ABB=ON PLU=ON L29 AND 6470650/BABSAN

=> d ide allref l31 1

L31 ANSWER 1 OF 22 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN): 9889295
Chemical Name (CN): <1-(<<2-(4-phenyl-1-piperazinyl)-4-pyrimidinyl>oxy>methyl)cyclobutyl>methyl (1S)-1-(oxo<<(1R)-1-

Autonom Name (AUN):	phenylethyl>amino>acetyl)pentylcarbamate <1-(1-phenyl-ethylaminooxalyl)-pentyl>-carbamic acid 1-<2-(4-phenyl-piperazin-1-yl)-pyrimidin-4-yloxymethyl>-cyclobutylmethyl ester
Molec. Formula (MF):	C36 H46 N6 O5
Molecular Weight (MW):	642.80
Lawson Number (LN):	29674, 28000, 14150, 14131, 5784, 3610, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8325784
Tautomer ID (TAUTID):	9261457
Entry Date (DED):	2005/04/22
Update Date (DUPD):	2005/04/22



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	7
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

NMR	Nuclear Magnetic Resonance	2
PHARM	Pharmacological Data	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Tavares, Francis X.; Deaton, David N.; Miller, Larry R.; Wright, Lois L., J. Med. Chem., CODEN: JMCMAR, 47(21), <2004>, 5057 - 5068; BABS-6470650

=> file babs
FILE 'BABS' ENTERED AT 17:08:39 ON 06 DEC 2006
COPYRIGHT (c) 2006 Beilstein-Institut zur Foerderung der Chemischen Wissenschaften licensed to Beilstein GmbH and MDL Information Systems GmbH

FILE LAST UPDATED: 25 SEP 2006 <20060925/UP>
FILE COVERS 1980 TO DATE.

=> d que l30
L30 8 SEA FILE=BABS ABB=ON PLU=ON (6470649/BABSAN OR 6470650/BABSAN OR 6462233/BABSAN OR 6498996/BABSAN OR 6021920/BABSAN OR 6080022/BABSAN OR 6410184/BABSAN OR 6437071/BABSAN)

=> d ibib abs l30 tot

L30 ANSWER 1 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: ***6498996*** BABS <<LOGINID::20061206>>
TITLE: A structural screening approach to ketoamide-based inhibitors of cathepsin K
AUTHOR(S): Barrett, David G.; Catalano, John G.; Deaton, David N.; Long, Stacey T.; McFadyen, Robert B.; Miller, Aaron B.; Miller, Larry R.; Wells-Knecht, Kevin J.; Wright, Lois L.
SOURCE: Bioorg. Med. Chem. Lett. (2005), 15(9), 2209 - 2214 CODEN: BMCLE8
DOCUMENT TYPE: Journal
AN ***6498996*** BABS <<LOGINID::20061206>>
AB Several novel ketoamide-based inhibitors of cathepsin K have been identified. Starting from a modestly potent inhibitor, structural screening of P2 elements led to 100-fold enhancements in inhibitory activity. Modifications to one of these leads resulted in an orally bioavailable cathepsin K inhibitor.

L30 ANSWER 2 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: ***6470650*** BABS <<LOGINID::20061206>>
TITLE: Ketoamide-Based Inhibitors of Cysteine Protease, Cathepsin K: P3 Modifications
AUTHOR(S): Tavares, Francis X.; Deaton, David N.; Miller, Larry R.; Wright, Lois L.
SOURCE: J. Med. Chem. (2004), 47(21), 5057 - 5068

CODEN: JMCMAR
DOCUMENT TYPE: Journal
AN *6470650* BABS <<LOGINID::20061206>>
AB Osteoporosis is a disease characterized by skeletal fragility. Cathepsin K, a lysosomal cysteine protease, has been implicated in the osteoclast mediated bone resorption. Inhibitors of this protease could potentially treat this skeletal disease. The present work describes exploration of the spatial requirements of the S3 subsite by the use of various sterically demanding P3 substituents. Sulfur and oxygen linked heterocycles as well as those without heteroatom linkers were found to provide potent inhibitors of cathepsin K. Representative examples from these series also afforded quite good selectivity ratios against most cathepsins tested. The tolerability of the S3 subsite for sterically demanding groups that provide potency and selectivity enhances the attractiveness of P3 changes to improve the physiochemical properties of inhibitors in the developments of compounds for the treatment of osteoporosis.

L30 ANSWER 3 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: *6470649* BABS <<LOGINID::20061206>>
TITLE: Potent and Selective Ketoamide-Based Inhibitors of Cysteine Protease, Cathepsin K
AUTHOR(S): Tavares, Francis X.; Deaton, David N.; Miller, Aaron B.; Miller, Larry R.; Wright, Lois L.; Zhou, Hui-Qiang
SOURCE: J. Med. Chem. (2004), 47(21), 5049 - 5056
CODEN: JMCMAR
DOCUMENT TYPE: Journal
AN *6470649* BABS <<LOGINID::20061206>>
AB Cathepsin K, a lysosomal cysteine protease of the papain superfamily, is abundantly and selectively expressed in osteoclasts, suggesting that this enzyme is crucial for bone resorption. Prevention of osteoclast-mediated bone resorption via inhibition of cathepsin K could be an effective approach to prevent osteoporosis. Potent and selective reversible ketoamide-based inhibitors have been identified in the present study. Using a known crystal structure of a ketoamide-based inhibitor, information from residues that form the P2/P3 pocket was used in the design of inhibitors that could allow for gains in selectivity and potency. Further, incorporation of P' selective heterocycles, along with the P2/P3 modifications, is also described. These modifications have resulted in potent and selective cathepsin K inhibitors that allow for improvements in their physiochemical properties and represent a viable lead series for the discovery of new therapies for the prevention and treatment of osteoporosis.

L30 ANSWER 4 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: *6462233* BABS <<LOGINID::20061206>>
TITLE: Potent and selective P%2&-P%3& ketoamide inhibitors of cathepsin K with good pharmacokinetic properties via favorable P%1'&, P%1&, and/or P%3& substitutions
AUTHOR(S): Barrett, David G.; Catalano, John G.; Deaton, David N.; Hassell, Anne M.; Long, Stacey T.; Miller, Aaron B.; Miller, Larry R.; Shewchuk, Lisa M.; Wells-Knecht, Kevin J.; Willard, Derril H.; Wright, Lois L.
SOURCE: Bioorg. Med. Chem. Lett. (2004), 14(19), 4897 - 4902
CODEN: BMCLE8
DOCUMENT TYPE: Journal
AN *6462233* BABS <<LOGINID::20061206>>
AB A series of ketoamides were synthesized and evaluated for inhibitory activity against cathepsin K. Exploration of the interactions between achiral P%2& substituents and the cysteine protease based on molecular

modelling suggestions resulted in potent cathepsin K inhibitors that demonstrated high selectivity versus cathepsin B, H, and L. Subsequent modifications of the P%3&, P%1&, and P%1'& moieties afforded orally bioavailable inhibitors.

L30 ANSWER 5 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: ***6437071*** BABS <<LOGINID::20061206>>
TITLE: Design of small molecule ketoamide-based inhibitors of cathepsin K
AUTHOR(S): Catalano, John G.; Deaton, David N.; Long, Stacey T.; McFadyen, Robert B.; Miller, Larry R.; Payne, J. Alan; Wells-Knecht, Kevin J.; Wright, Lois L.
SOURCE: Bioorg.Med.Chem.Lett. (2004), 14(3), 719 - 722
CODEN: BMCLE8
DOCUMENT TYPE: Journal
LANGUAGE: English
SUMMARY LANGUAGE: English
AN ***6437071*** BABS <<LOGINID::20061206>>
AB A novel series of ketoamide-based inhibitors of cathepsin K has been identified. Modifications to P%2& and P%3& elements were crucial to enhancing inhibitory activity. Although not optimized, a selected inhibitor was effective in attenuating type I collagen hydrolysis in a surrogate assay of bone resorption.

L30 ANSWER 6 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: ***6410184*** BABS <<LOGINID::20061206>>
TITLE: Application of acyl cyanophosphorane methodology to the synthesis of protease inhibitors: poststatin, eurystatin, phebestin, probestin and bestatin
AUTHOR(S): Wasserman, Harry H.; Petersen, Anders K.; Xia, Mingle
SOURCE: Tetrahedron (2003), 59(35), 6771 - 6784
CODEN: TETRAB
DOCUMENT TYPE: Journal
LANGUAGE: English
SUMMARY LANGUAGE: English
AN ***6410184*** BABS <<LOGINID::20061206>>
AB Full details are given for the syntheses of the protease inhibitors, poststatin and eurystatin by the acyl cyanophosphorane coupling procedure used for the formation of $a-keto amides. We have also extended this methodology to the syntheses of the related $a-hydroxy amide natural products, phebestin, probestin and bestatin. The key step in the latter synthetic sequences involved diastereomeric selectivity in the reduction of the $a-keto precursor to the corresponding $a-hydroxy amide by the use of zinc borohydride.

L30 ANSWER 7 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: ***6080022*** BABS <<LOGINID::20061206>>
TITLE: Synthesis of the Cyclic Peptidic Protease Inhibitor Eurystatin A Using Acyl Cyano Phosphorane Methodology
AUTHOR(S): Wasserman, Harry H.; Petersen, Anders K.
SOURCE: J.Org.Chem. (1997), 62(26), 8972-8973
CODEN: JOCEAH
DOCUMENT TYPE: Journal
LANGUAGE: English
AN ***6080022*** BABS <<LOGINID::20061206>>

L30 ANSWER 8 OF 8 BABS COPYRIGHT 2006 BEILSTEIN MDL on STN
ACCESSION NUMBER: ***6021920*** BABS <<LOGINID::20061206>>
TITLE: Poststatin, a New Inhibitor of Prolyl Endopeptidase

VI.Endopeptidase Inhibitory Activity of Poststatin Analogues Containing Pyrrolidine Ring

AUTHOR(S): Tsuda, Makoto; Muraoka, Yasuhiko; Someno, Tetsuya; Nagai, Machiko; Aoyagi, Takaaki; Takeuchi, Tomio

SOURCE: J.Antibiot. (1996), 49(9), 900-908
CODEN: JANTAJ
DOCUMENT TYPE: Journal
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Several pyrrolidine-containing analogues of poststatin were synthesized and examined for their inhibitory activity against prolyl endopeptidase and cathepsin B in vitro.Replacement of the postine residue with 2-oxo-2-(2-pyrrolidinyl)acetic acid increased the selectivity and inhibitory activity against prolyl endopeptidase.Benzyloxacarbonyl-L-phenylalanyl-(S)-2-oxo-2-(2-pyrrolidinyl)acetyl-D-phenylalanine was about 46 times as active to prolyl endopeptidase as natural poststatin.